Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners on the optimal use of ARV agents for the treatment of HIV infection in adults and adolescents in the United States.
Panel members	The Panel is composed of more than 30 voting members who have expertise in HIV care and research. The U.S. government representatives include at least 1 representative from each of the following DHHS agencies: Centers for Disease Control and Prevention (CDC), FDA, Health Resource Services Administration (HRSA), and National Institutes of Health (NIH). These members are appointed by their respective agencies. Approximately 2/3 of the Panel members are nongovernmental scientific members. There are 4–5 community members with knowledge in HIV treatment and care. Members who do not represent U.S. government agencies are selected after an open announcement to call for nominations. Each member serves on the Panel for a 4-year term, with an option to be reappointed for an additional term. A list of the current members can be found on Page vii of this document.
Financial disclosures	All members of the Panel submit a written financial disclosure annually reporting any association with manufacturers of ARV drugs or diagnostics used for management of HIV infections. A list of the latest disclosures is available.
Users of the guidelines	HIV treatment providers
Developer	Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of OARAC
Funding source	Office of AIDS Research, NIH
Evidence collection	The recommendations in the guidelines are generally based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2.
Method of synthesizing data	Each section of the guidelines is assigned to a working group of Panel members with expertise in the area of interest. The members of the working group synthesize the available data and propose recommendations to the Panel. All proposals are discussed at monthly teleconferences and then voted on by the Panel before being endorsed as official recommendations.
Other guidelines	These guidelines focus on treatment for HIV-infected adults and adolescents. Separate guidelines outline the use of ART for other populations, such as pregnant women and children. These guidelines are also available on the AIDS*info* Web site (http://www.aidsinfo.nih.gov). There is a brief discussion of the management of women of reproductive age and pregnant women in this document. For a more detailed and up-to-date discussion on this group of women and other special populations, the Panel defers to the designated expertise offered by panels that have developed those guidelines.
Update plan	The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency), new significant safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. For cases in which significant new data become available that may affect patient safety, a warning announcement with the Panel's recommendations may be made on the AIDS*info* Web site until appropriate changes can be made in the guidelines document. Updated guidelines are available on the AIDS*info* Web site (http://www.aidsinfo.nih.gov).
Public comments	After release of an update on the AIDS*info* Web site, the public is given a 2-week period to submit comments to the Panel. These comments are reviewed, and a determination is made as to whether revisions are indicated. The public may also submit comments to the Panel at any time at contactus@aidsinfo.nih.gov.

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement **B:** Moderate recommendation for the statement **C:** Optional recommendation for the statement	**I:** One or more randomized trials with clinical outcomes and/or validated laboratory endpoints **II:** One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes **III:** Expert opinion

Table 3. Laboratory Monitoring Schedule for Patients Prior to and After Initiation of Antiretroviral Therapy

	Entry into care	Follow-up before ART	ART initiation or modification[a]	2–8 weeks post-ART initiation or modification	Every 3–6 months	Every 6 months	Every 12 months	Treatment failure	Clinically indicated
CD4 count	√	every 3–6 months	√		√	In clinically stable patients with suppressed viral load, CD4 count can be monitored every 6–12 months (see text)		√	√
Viral load	√	every 3–6 months	√	√[b]	√[c]			√	√
Resistance testing	√		√[d]					√	√
HLA-B*5701 testing			√ if considering ABC						
Tropism testing			√ if considering a CCR5 antagonist					√ if considering a CCR5 antagonist or for failure of CCR5 antagonist-based regimen	√
Hepatitis B serology[e]	√		√ may repeat if HBsAg (-) and HBsAb (-) at baseline						√
Basic chemistry[f]	√	every 6–12 months	√	√	√				√
ALT, AST, T. bilirubin	√	every 6–12 months	√	√	√				√
CBC with differential	√	every 3–6 months	√	√ if on ZDV	√				√
Fasting lipid profile	√	if normal, annually	√	√ consider 4–8 weeks after starting new ART		√ if abnormal at last measurement	√ if normal at last measurement		√
Fasting glucose	√	if normal, annually	√		√ if abnormal at last measurement	√ if normal at last measurement			√
Urinalysis[g]	√		√			√ if on TDF[h]	√		√
Pregnancy test			√ if starting EFV						√

Table 3, continued. Laboratory Monitoring Schedule for Patients Prior to and After Initiation of Antiretroviral Therapy

[a] ARV modification may be done for treatment failure, adverse effects, or simplification.

[b] If HIV RNA is detectable at 2–8 weeks, repeat every 4–8 weeks until suppression to <200 copies/mL, then every 3–6 months.

[c] For adherent patients with suppressed viral load and stable clinical and immunologic status for >2–3 years, some experts may extend the interval for HIV RNA monitoring to every 6 months.

[d] For ART-naive patients, if resistance testing was performed at entry into care, repeat testing is optional; for patients with viral suppression who are switching therapy for toxicity or convenience, resistance testing will not be possible and therefore is not necessary.

[e] If HBsAg is positive at baseline or prior to initiation of ART, TDF + (FTC or 3TC) should be used as part of ARV regimen to treat both HBV and HIV infections. If HBsAg and HBsAb are negative at baseline, hepatitis B vaccine series should be administered.

[f] Serum Na, K, HCO^3, Cl, BUN, creatinine, glucose (preferably fasting); some experts suggest monitoring phosphorus while on TDF; determination of renal function should include estimation of creatinine clearance using Cockcroft-Gault equation or estimation of glomerular filtration rate based on MDRD equation.

[g] For patients with renal disease, consult "Guidelines for the Management of Chronic Kidney Disease in HIV-Infected Patients: Recommendations of the HIV Medicine Association of the Infectious Diseases Society of America".[1]

[h] More frequent monitoring may be indicated for patients with increased risk of renal insufficiency, such as patients with diabetes, hypertension, etc.

Acronyms: 3TC = lamivudine, ABC = abacavir, ALT = alanine aminotransferase, ART = antiretroviral therapy, AST = aspartate aminotranserase, CBC = complete blood count, EFV = efavirenz, FTC = emtricitabine, HBsAb = hepatitis B surface antibody, HBsAg = hepatitis B surface antigen, HBV = hepatitis B virus, MDRD = modification of diet in renal disease (equation), TDF = tenofovir, ZDV = zidovudine

Table 4. Recommendations for Using Drug-Resistance Assays
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Clinical Setting/Recommendation	Rationale
Drug-resistance assay recommended	
In acute HIV infection: Drug-resistance testing is recommended regardless of whether ART is initiated immediately or deferred **(AIII)**. A genotypic assay is generally preferred **(AIII)**.	If ART is to be initiated immediately, drug-resistance testing will determine whether drug-resistant virus was transmitted. Test results will help in the design of initial regimens or to modify or change regimens if results are obtained subsequent to treatment initiation. Genotypic testing is preferable to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If ART is deferred, repeat resistance testing should be considered at the time therapy is initiated **(CIII)**. A genotypic assay is generally preferred **(AIII)**.	If ART is deferred, testing should still be performed because of the greater likelihood that transmitted resistance-associated mutations will be detected earlier in the course of HIV infection. Results of resistance testing may be important when treatment is initiated. Repeat testing at the time ART is initiated should be considered because the patient may have acquired a drug-resistant virus (i.e., superinfection).
In ART-naive patients with chronic HIV infection: Drug-resistance testing is recommended at the time of entry into HIV care, regardless of whether therapy is initiated immediately or deferred **(AIII)**. A genotypic assay is generally preferred **(AIII)**.	Transmitted HIV with baseline resistance to at least one drug is seen in 6%–16% of patients, and suboptimal virologic responses may be seen in patients with baseline resistant mutations. Some drug-resistance mutations can remain detectable for years in untreated chronically infected patients.
If therapy is deferred, repeat resistance testing should be considered prior to the initiation of ART **(CIII)**. A genotypic assay is generally preferred **(AIII)**.	Repeat testing prior to initiation of ART should be considered because the patient may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferable to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If an INSTI is considered for an ART-naive patient and transmitted INSTI resistance is a concern, providers may wish to supplement standard resistance testing with a specific INSTI genotypic resistance assay **(CIII)**.	Standard genotypic drug-resistance assays test only for mutations in the RT and PR genes.
In patients with virologic failure: Drug-resistance testing is recommended in persons on combination ART with HIV RNA levels >1,000 copies/mL **(AI)**. In persons with HIV RNA levels >500 but <1,000 copies/mL, testing may be unsuccessful but should still be considered **(BII)**.	Testing can help determine the role of resistance in drug failure and maximize the clinician's ability to select active drugs for the new regimen. Drug-resistance testing should be performed while the patient is taking prescribed ARV drugs or, if not possible, within 4 weeks after discontinuing therapy.
A standard genotypic resistance assay is generally preferred for those experiencing virologic failure on their first or second regimens **(AIII)**.	Genotypic testing is preferable to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
In patients failing INSTI-based regimens, genotypic testing for INSTI resistance should be considered to determine whether to include drugs from this class in subsequent regimens **(BIII)**.	Standard genotypic drug-resistance assays test only for mutations in the RT and PR genes.

Table 4. Recommendations for Using Drug-Resistance Assays
Page 2 of 2

Clinical Setting/Recommendation	Rationale
Drug-resistance assay recommended	
Addition of phenotypic assay to genotypic assay is generally preferred for those with known or suspected complex drug-resistance patterns, particularly to PIs **(BIII)**.	Phenotypic testing can provide useful additional information for those with complex drug-resistance mutation patterns, particularly to PIs.
In patients with suboptimal suppression of viral load: Drug-resistance testing is recommended for persons with suboptimal suppression of viral load after initiation of ART **(AII)**.	Testing can help determine the role of resistance and thus assist the clinician in identifying the number of active drugs available for a new regimen.
In HIV-infected pregnant women: Genotypic resistance testing is recommended for all pregnant women prior to initiation of ART **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI)**.	The goal of ART in HIV-infected pregnant women is to achieve maximal viral suppression for treatment of maternal HIV infection and for prevention of perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal regimen for the patient.
Drug-resistance assay not usually recommended	
After therapy discontinued: Drug-resistance testing is not usually recommended after discontinuation (>4 weeks) of ARV drugs **(BIII)**.	Drug-resistance mutations might become minor species in the absence of selective drug pressure, and available assays might not detect minor drug-resistant species. If testing is performed in this setting, the detection of drug resistance may be of value; however, the absence of resistance does not rule out the presence of minor drug-resistant species.
In patients with low HIV RNA levels: Drug-resistance testing is not usually recommended in persons with a plasma viral load <500 copies/mL **(AIII)**.	Resistance assays cannot be consistently performed given low HIV RNA levels.

Table 5a. Preferred and Alternative Antiretroviral Regimens for Antiretroviral Therapy-Naive Patients

A combination ART regimen generally consists of two NRTIs + one active drug from one of the following classes: NNRTI, PI (generally boosted with RTV), INSTI, or a CCR5 antagonist. Selection of a regimen should be individualized on the basis of virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, and the patient's comorbid conditions. Refer to Table 6 for a list of advantages and disadvantages and Appendix B, Tables 1–6 for dosing information for individual ARV agents listed below. The regimens in each category are listed in alphabetical order.

Preferred Regimens (Regimens with optimal and durable efficacy, favorable tolerability and toxicity profile, and ease of use) The preferred regimens for non-pregnant patients are arranged by chronological order of FDA approval of components other than nucleosides and, thus, by duration of clinical experience.	
NNRTI-Based Regimen • EFV/TDF/FTC[a] **(AI)** *PI-Based Regimens (in alphabetical order)* • ATV/r + TDF/FTC[a] **(AI)** • DRV/r (once daily) + TDF/FTC[a] **(AI)** *INSTI-Based Regimen* • RAL + TDF/FTC[a] **(AI)** *Preferred Regimen for Pregnant Women*[b] • LPV/r (twice daily) + ZDV/3TC[a] **(AI)**	*Comments* **EFV** should not be used during the first trimester of pregnancy or in women of childbearing potential who are trying to conceive or not using effective and consistent contraception. **TDF** should be used with caution in patients with renal insufficiency. **ATV/r** should not be used in patients who require >20 mg omeprazole equivalent per day. Refer to Table 15a for dosing recommendations regarding interactions between ATV/r and acid-lowering agents.
Alternative Regimens (Regimens that are effective and tolerable but have potential disadvantages compared with preferred regimens. An alternative regimen may be the preferred regimen for some patients.)	
NNRTI-Based Regimens (in alphabetical order) • EFV + ABC/3TC[a] **(BI)** • RPV/TDF/FTC[a] **(BI)** • RPV + ABC/3TC[a] **(BIII)** *PI-Based Regimens (in alphabetical order)* • ATV/r + ABC/3TC[a] **(BI)** • DRV/r + ABC/3TC[a] **(BIII)** • FPV/r (once or twice daily) + ABC/3TC[a] or TDF/FTC[a] **(BI)** • LPV/r (once or twice daily) + ABC/3TC[a] or TDF/FTC[a] **(BI)** *INSTI-Based Regimen* • RAL + ABC/3TC[a] **(BIII)**	*Comments* • Use **RPV** with caution in patients with pretreatment HIV RNA >100,000 copies/mL. • Use of PPIs with **RPV** is contraindicated. • **ABC** should not be used in patients who test positive for HLA-B*5701. • Use **ABC** with caution in patients with known high risk of CVD or with pretreatment HIV RNA >100,000 copies/mL. (See text.) **Once-daily LPV/r** is not recommended for use in pregnant women.

[a] 3TC may substitute for FTC or vice versa.

[b] For more detailed recommendations on ARV use in an HIV-infected pregnant woman, refer to the perinatal guidelines available at http://aidsinfo.nih.gov/guidelines.

The following combinations in the recommended list above are available as coformulated fixed-dose combinations: ABC/3TC, EFV/TDF/FTC, LPV/r, RPV/TDF/FTC, TDF/FTC, and ZDV/3TC.

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ART = antiretroviral therapy, ARV = antiretroviral, ATV/r = atazanavir/ritonavir, CVD = cardiovascular disease, DRV/r = darunavir/ritonavir, EFV = efavirenz, FDA = Food and Drug Administration, FPV/r = fosamprenavir/ritonavir, FTC = emtricitabine, INSTI = integrase strand transfer inhibitor, LPV/r = lopinavir/ritonavir, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleos(t)ide reverse transcriptase inhibitor, PI = protease inhibitor, PPI = proton pump inhibitor, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, TDF = tenofovir, ZDV = zidovudine

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Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion*

Table 5b. Acceptable Antiretroviral Regimens for Treatment-Naive Patients

Acceptable Regimens (CI) (Regimens that may be selected for some patients but are less satisfactory than preferred or alternative regimens) **and Regimens that may be acceptable but more definitive data are needed (CIII)**	
NNRTI-Based Regimen • EFV + ZDV/3TC[a] **(CI)** • NVP + (TDF/FTC[a] or ZDV/3TC[a]) **(CI)** • NVP + ABC/3TC[a] **(CIII)** • RPV + ZDV/3TC[a] **(CIII)** *PI-Based Regimens* • ATV + (ABC or ZDV)/3TC[a] **(CI)** • ATV/r + ZDV/3TC[a] **(CI)** • DRV/r + ZDV/3TC[a] **(CIII)** • FPV/r + ZDV/3TC[a] **(CI)** • LPV/r + ZDV/3TC[a] **(CIII)** *INSTI-Based Regimen* • RAL + ZDV/3TC[a] **(CIII)** *CCR5 Antagonist-Based Regimens* • MVC + ZDV/3TC[a] **(CI)** • MVC + TDF/FTC[a] or ABC/3TC[a] **(CIII)**	*Comments* • **NVP** should not be used in patients with moderate to severe hepatic impairment (Child-Pugh B or C).[b] • **NVP** should not be used in women with pre-ART CD4 count >250 cells/mm^3 or in men with pre-ART CD4 count >400 cells/mm^3. Use **NVP** and **ABC** together with caution because both can cause HSRs within the first few weeks after initiation of therapy. **ZDV** can cause bone marrow suppression, lipoatrophy, and rarely lactic acidosis with hepatic steatosis. **LPV/r (twice daily) + ZDV/3TC** is the preferred regimen for use in pregnant women. **ATV/r** is generally preferred over **unboosted ATV**. **Unboosted ATV** may be used when RTV boosting is not possible. Perform tropism testing before initiation of therapy with **MVC**. **MVC** may be considered in patients who have only CCR5-tropic virus.
Regimens that may be acceptable but should be used with caution (Regimens that have demonstrated virologic efficacy in some studies but are associated with concerns about safety, resistance, or efficacy. See comments below.)	
PI-Based Regimens • SQV/r + TDF/FTC[a] **(CI)** • SQV/r + (ABC or ZDV)/3TC[a] **(CIII)**	*Comments* • **SQV/r** was associated with PR and QT prolongation in a healthy volunteer study. • Baseline ECG is recommended before initiation of **SQV/r**. • **SQV/r** is not recommended in patients with any of the following: 1. pretreatment QT interval >450 msec 2. refractory hypokalemia or hypomagnesemia 3. concomitant therapy with other drugs that prolong QT interval 4. complete AV block without implanted pacemaker 5. risk of complete AV block

[a] 3TC may substitute for FTC or vice versa.
[b] Refer to Appendix B, Table 7 for the criteria for Child-Pugh classification

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ART = antiretroviral therapy, ATV = atazanavir, ATV/r = atazanavir/ritonavir, AV = atrioventricular, DRV/r = darunavir/ritonavir, ECG = electrocardiogram, EFV = efavirenz, FPV/r = fosamprenavir/ ritonavir, FTC = emtricitabine, HSR = hypersensitivity reaction, INSTI = integrase strand transfer inhibitor, LPV/r = lopinavir/ ritonavir, msec = millisecond, MVC = maraviroc, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PI = protease inhibitor, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SQV/r = saquinavir/ritonavir, TDF = tenofovir, ZDV = zidovudine

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Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*

Rating of Evidence: *I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion*

Table 6. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 1 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
NNRTIs (in alphabetical order)		**NNRTI Class Advantages:** • Long half-lives	**NNRTI Class Disadvantages:** • Greater risk of resistance at the time of treatment failure with NNRTIs than with PIs • Potential for cross resistance • Skin rash • Potential for CYP450 drug interactions (See Tables 14, 15b, and 16b.) • Transmitted resistance more common with NNRTIs than with PIs
	EFV	• Virologic responses equivalent or superior to all comparators to date • Once-daily dosing • Coformulated with TDF/FTC	• Neuropsychiatric side effects • Teratogenic in nonhuman primates. Several cases of neural tube defect in infants born to women who were exposed to EFV in the first trimester of pregnancy reported. EFV use should be avoided in women with potential for pregnancy and is contraindicated in the first trimester. • Dyslipidemia
	NVP	• No food effect • Fewer lipid effects than EFV • Once-daily dosing with extended-release tablet formulation	• Higher incidence of rash, including rare but serious HSRs (SJS or TEN), than with other NNRTIs • Higher incidence of hepatotoxicity, including serious and even fatal cases of hepatic necrosis, than with other NNRTIs • Contraindicated in patients with moderate or severe (Child-Pugh B or C) hepatic impairment • Some data suggest that ART-naive patients with high pre-NVP CD4 counts (>250 cells/mm^3 for females, >400 cells/mm^3 for males) are at higher risk of symptomatic hepatic events. NVP is not recommended in these patients unless benefit clearly outweighs risk. • Early virologic failure of NVP + TDF + (FTC or 3TC) in small clinical trials

	RPV	• Once-daily dosing
		• Coformulated with TDF/FTC
		• Compared with EFV:
		  • Fewer discontinuations for CNS adverse effects
		  • Fewer lipid effects
		  • Fewer rashes
			• More virologic failures in patients with pretreatment HIV RNA >100,000 copies/mL than with EFV-based regimen
			• More NNRTI- and 3TC-associated mutations at virological failure than with regimen containing EFV + two NRTIs
			• Food requirement
			• Absorption depends on lower gastric pH. (See Table 15a for detailed information regarding interactions with H2 antagonists and antacids.)
			• Contraindicated with PPIs
			• RPV-associated depression reported
			• Use RPV with caution when coadministered with a drug having a known risk of torsades de pointes.

Table 6. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 2 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
PIs (in alphabetical order)		**PI Class Advantages:** • Higher genetic barrier to resistance than NNRTIs and RAL • PI resistance uncommon with failure while on first PI regimen	**PI Class Disadvantages:** • Metabolic complications such as dyslipidemia, insulin resistance, hepatotoxicity • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (more pronounced with RTV-based regimens) (See Tables 14 and 15a.)
	ATV	• Fewer adverse effects on lipids than other PIs • Once-daily dosing • Low pill burden • Good GI tolerability • Signature mutation (I50L) not associated with broad PI cross resistance	• Indirect hyperbilirubinemia sometimes leading to jaundice or scleral icterus • PR interval prolongation: generally inconsequential unless ATV combined with another drug with similar effect • Cannot be coadministered with TDF, EFV, or NVP (See ATV/r.) • Nephrolithiasis • Skin rash • Food requirement • Absorption depends on food and low gastric pH. (See Table 15a for detailed information regarding interactions with H2 antagonists, antacids, and PPIs.)
	ATV/r	• RTV boosting: higher trough ATV concentration and greater antiviral effect • Once-daily dosing • Low pill burden	• More adverse effects on lipids than unboosted ATV • More hyperbilirubinemia and jaundice than unboosted ATV • Food requirement • Absorption depends on food and low gastric pH. (See Table 15a for interactions with H2 antagonists, antacids, and PPIs.) • RTV boosting required with TDF and EFV. With EFV, use ATV 400 mg and RTV 100 mg once daily (PI-naive patients only). • Should not be coadministered with NVP
	DRV/r	• Once-daily dosing • Potent virologic efficacy	• Skin rash • Food requirement
	FPV/r	• Twice-daily dosing resulted in efficacy comparable to LPV/r • RTV boosting results in higher trough APV concentration and greater antiviral effect • Once-daily dosing possible with RTV 100 mg or 200 mg daily • No food effect	• Skin rash • Hyperlipidemia • Once-daily dosing results in lower APV concentrations than twice-daily dosing • For FPV 1400 mg + RTV 200 mg: requires 200 mg of RTV and no coformulation • Fewer data on FPV 1400 mg + RTV 100 mg dose than on DRV/r and ATV/r

Table 6. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 3 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
PIs (in alphabetical order)	**LPV/r**	• Coformulated • No food requirement • Recommended PI in pregnant women (twice daily only) • Greater CD4 count increase than with EFV-based regimens	• Requires 200 mg per day of RTV • Lower drug exposure in pregnant women—may need dose increase in third trimester • Once-daily dosing not recommended in pregnant women • Once-daily dosing results in lower trough concentration than twice-daily dosing • Possible higher risk of MI associated with cumulative use of LPV/r • PR and QT interval prolongation have been reported. Use with caution in patients at risk of cardiac conduction abnormalities or receiving other drugs with similar effect.
	SQV/r	• Similar efficacy but less hyperlipidemia than with LPV/r	• Highest pill burden (6 pills per day) among available PI regimens • Requires 200 mg of RTV • Food requirement • PR and/or QT interval prolongations in a healthy volunteer study • Pretreatment ECG recommended • SQV/r is not recommended for patients with any of the following conditions: (1) congenital or acquired QT prolongation; (2) pretreatment ECG >450 msec; (3) on concomitant therapy with other drugs that prolong QT interval; (4) complete AV block without implanted pacemakers; (5) risk of complete AV block.
INSTI	**RAL**	• Virologic response noninferior to EFV • Fewer drug-related adverse events and lipid changes than EFV • No food effect • Fewer drug-drug interactions than PI- or NNRTI-based regimens	• Twice-daily dosing • Lower genetic barrier to resistance than with boosted PI-based regimens • No data with NRTIs other than TDF/FTC in ART-naive patients • Increase in creatine kinase, myopathy, and rhabdomyolysis have been reported • Rare cases of severe skin reactions (including SJS and TEN) have been reported and systemic HSRs with rash and constitutional symptoms, with or without hepatitis, have been reported.
CCR5 Antagonist	**MVC**	• Virologic response noninferior to EFV in post hoc analysis of MERIT study (See text.) • Fewer adverse effects than EFV	• Requires viral tropism testing prior to initiation of therapy, which results in additional cost and possible delay in initiation of therapy • More MVC-treated than EFV-treated patients discontinued therapy due to lack of efficacy in MERIT study • Less long-term experience in ART-naive patients than with boosted PI- or NNRTI-based regimens • Limited experience with dual-NRTIs other than ZDV/3TC • Twice-daily dosing • CYP 3A4 substrate; dosing depends on presence or absence of concomitant CYP3A4 inducer(s) or inhibitor(s)

Table 6. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy (page 4 of 4)

ARV Class	ARV Agent(s)	Advantages	Disadvantages
Dual-NRTI pairs (in alphabetical order)	**ABC/3TC**	• Virologic response noninferior to ZDV/3TC • Better CD4 count responses than with ZDV/3TC • Once-daily dosing • Coformulation • No food effect • No cumulative TAM-mediated resistance	• Potential for ABC HSR in patients with HLA-B*5701 • Increased potential for cardiovascular events, especially in patients with cardiovascular risk factors • Inferior virologic responses in patients with baseline HIV RNA >100,000 copies/mL when compared with TDF/FTC in ACTG 5202 study; however, this was not seen in the HEAT study.
	TDF/FTC	• Better virologic responses than with ZDV/3TC • Better virologic responses than with ABC/3TC in patients with baseline HIV RNA >100,000 copies/mL in ACTG 5202 study; however, this was not seen in the HEAT study. • Active against HBV; recommended dual-NRTI for HIV/HBV coinfection • Once-daily dosing • No food effect • Coformulated (TDF/FTC, EFV/TDF/FTC, and RPV/TDF/FTC) • No cumulative TAM-mediated resistance	• Potential for renal impairment, including Fanconi syndrome and acute renal insufficiency • Early virologic failure of NVP + TDF + (FTC or 3TC) in small clinical trials • Potential for decrease in BMD
	ZDV/3TC	• Coformulated (ZDV/3TC and ZDV/3TC/ABC) • No food effect (although better tolerated with food) • Preferred dual NRTI in pregnant women	• Bone marrow suppression, especially anemia and neutropenia • GI intolerance, headache • Mitochondrial toxicity, including lipoatrophy, lactic acidosis, hepatic steatosis • Compared with TDF/FTC, inferior in combination with EFV • Less CD4 increase compared with ABC/3TC • Twice-daily dosing

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, APV = amprenavir, ART = antiretroviral therapy, ARV = antiretroviral, ATV = atazanavir, ATV/r = atazanavir/ritonavir, AV = atrioventricular, BMD = bone mineral density, CNS = central nervous system, CYP = cytochrome P, d4T = stavudine, ddI = didanosine, DRV/r = darunavir/ritonavir, ECG = electrocardiogram, EFV = efavirenz, FPV = fosamprenavir, FPV/r = fosamprenavir/ ritonavir, FTC = emtricitabine, GI = gastrointestinal, HBV = hepatitis B virus, HSR = hypersensitivity reaction, INSTI = integrase strand transfer inhibitor, LPV/r = lopinavir/ritonavir, MI = myocardial infarction, msec = milliseconds, MVC = maraviroc, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PI = protease inhibitor, PPI = proton pump inhibitor, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SJS = Stevens-Johnson syndrome, SQV/r = saquinavir/ritonavir, TAM = thymidine analogue mutation, TDF = tenofovir, TEN = toxic epidermal necrosis, ZDV = zidovudine

Table 7. Antiretroviral Components or Regimens Not Recommended as Initial Therapy

ARV drugs or components (in alphabetical order)	Reasons for NOT recommending as initial therapy
ABC/3TC/ZDV (coformulated) as triple-NRTI combination regimen **(BI)**	• Inferior virologic efficacy
ABC + 3TC + ZDV + TDF as quadruple-NRTI combination regimen **(BI)**	• Inferior virologic efficacy
DRV (unboosted)	• Use without RTV has not been studied
DLV **(BIII)**	• Inferior virologic efficacy • Inconvenient (three times daily) dosing
ddI + 3TC (or FTC) **(BIII)**	• Inferior virologic efficacy • Least clinical trial experience in ART-naive patients
ddI + TDF **(BII)**	• High rate of early virologic failure • Rapid selection of resistance mutations • Potential for immunologic nonresponse/CD4 T-cell decline • Increased ddI drug exposure and toxicities
T20 **(BIII)**	• No clinical trial experience in ART-naive patients • Requires twice-daily subcutaneous injections
ETR **(BIII)**	• Insufficient data in ART-naive patients
FPV (unboosted) **(BIII)**	• Less potent than RTV-boosted FPV • Virologic failure with unboosted FPV-based regimen may select mutations that confer resistance to DRV
IDV (unboosted) **(BIII)**	• Inconvenient dosing (three times daily with meal restrictions) • Fluid requirement
IDV (RTV-boosted) **(BIII)**	• High incidence of nephrolithiasis
NFV **(BI)**	• Inferior virologic efficacy • High incidence of diarrhea
RTV as sole PI **(BIII)**	• High pill burden • GI intolerance
SQV (unboosted) **(BI)**	• Inferior virologic efficacy
d4T + 3TC **(BI)**	• Significant toxicities including lipoatrophy; peripheral neuropathy; and hyperlactatemia, including symptomatic and life-threatening lactic acidosis, hepatic steatosis, and pancreatitis
TPV (RTV-boosted) **(BI)**	• Inferior virologic efficacy

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ART = antiretroviral therapy, ARV = antiretroviral, d4T = stavudine, ddI = didanosine, DLV = delavirdine, DRV = darunavir, ETR = etravirine, FPV = fosamprenavir, FTC = emtricitabine, GI = gastrointestinal, IDV = indinavir, NFV = nelfinavir, NRTI = nucleoside reverse transcriptase inhibitor, PI = protease inhibitor, RTV = ritonavir, SQV = saquinavir, T20 = enfuvirtide, TDF = tenofovir, TPV = tipranavir, ZDV = zidovudine

Table 8. Antiretroviral Regimens or Components That Should Not Be Offered At Any Time (page 1 of 2)

	Rationale	Exception
Antiretroviral Regimens Not Recommended		
Monotherapy with NRTI (AII)	• Rapid development of resistance • Inferior ARV activity when compared with combination of three or more ARV agents	• No exception
Dual-NRTI regimens (AI)	• Rapid development of resistance • Inferior ARV activity when compared with combination of three or more ARV agents	• No exception
Triple-NRTI regimens (AI) except for ABC/ZDV/3TC (BI) or possibly TDF + ZDV/3TC (BII)	• High rate of early virologic nonresponse seen when triple-NRTI combinations, including ABC/TDF/3TC and TDF/ddI/3TC, were used as initial regimen in ART-naive patients. • Other triple-NRTI regimens have not been evaluated.	• ABC/ZDV/3TC **(BI)** and possibly TDF + ZDV/3TC **(BII)** in patients in whom other combinations are not desirable
Antiretroviral Components Not Recommended as Part of an Antiretroviral Regimen		
ATV + IDV (AIII)	• Potential additive hyperbilirubinemia	• No exception
ddI + d4T (AII)	• High incidence of toxicities: peripheral neuropathy, pancreatitis, and hyperlactatemia • Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis with or without pancreatitis in pregnant women	• No exception
ddI + TDF (AII)	• Increased ddI concentrations and serious ddI-associated toxicities • Potential for immunologic nonresponse and/or CD4 cell count decline • High rate of early virologic failure • Rapid selection of resistance mutations at failure	• Clinicians caring for patients who are clinically stable on regimens containing TDF + ddI should consider altering the NRTIs to avoid this combination.
2-NNRTI combination (AI)	• When EFV combined with NVP, higher incidence of clinical adverse events seen when compared with either EFV- or NVP-based regimen. • Both EFV and NVP may induce metabolism and may lead to reductions in ETR exposure; thus, they should not be used in combination with ETR.	• No exception
EFV in first trimester of pregnancy or in women with significant childbearing potential (AIII)	• Teratogenic in nonhuman primates	• When no other ARV options are available and potential benefits outweigh the risks **(BIII)**
FTC + 3TC (AIII)	• Similar resistance profiles • No potential benefit	• No exception
ETR + unboosted PI (AII)	• ETR may induce metabolism of these PIs; appropriate doses not yet established	• No exception
ETR + RTV-boosted ATV or FPV (AII)	• ETR may alter the concentrations of these PIs; appropriate doses not yet established	• No exception
ETR + RTV-boosted TPV (AII)	• ETR concentration may be significantly reduced by RTV-boosted TPV	• No exception

Table 8. Antiretroviral Regimens or Components That Should Not Be Offered At Any Time (page 2 of 2)

	Rationale	Exception
NVP in ARV-naive women with CD4 count >250 cells/mm^3 or men with CD4 count >400 cells/mm^3 (BI)	• High incidence of symptomatic hepatotoxicity	• If no other ARV option available; if used, patient should be closely monitored
d4T + ZDV (AII)	• Antagonistic effect on HIV-1	• No exception
Unboosted DRV, SQV, or TPV (AII)	• Inadequate bioavailability	• No exception

Acronyms: 3TC = lamivudine, ABC = abacavir, ATV = atazanavir, d4T = stavudine, ddI = didanosine, DRV = darunavir, EFV = efavirenz, ETR = etravirine, FPV = fosamprenavir, FTC = emitricitabine, IDV = indinavir, NVP = nevirapine, RTV = ritonavir, SQV = saquinavir, TDF = tenofovir, TPV = tipranavir, ZDV = zidovudine

Table 9a. Trough Concentrations of Antiretroviral Drugs for Patients Who Have Drug-Susceptible Virus

Drug	Concentration (ng/mL)
Suggested minimum target trough concentrations in patients with HIV-1 susceptible to the ARV drugs[2-9]	
Fosamprenavir (FPV)	400 (measured as amprenavir concentration)
Atazanavir (ATV)	150
Indinavir (IDV)	100
Lopinavir (LPV)	1000
Nelfinavir[a] (NFV)	800
Saquinavir (SQV)	100–250
Efavirenz (EFV)	1000
Nevirapine (NVP)	3000

[a] Measurable active (M8) metabolite

Table 9b. Trough Concentrations of Antiretroviral Drugs for Treatment-Experienced Patients with Virologic Failure

Drug	Concentration (ng/mL)
Suggested minimum target trough concentrations for ART-experienced patients who have resistant HIV-1 strains	
Maraviroc (MVC)	>50
Tipranavir (TPV)	20,500
Median (Range) Trough Concentrations from Clinical Trials[12-14]	
Darunavir (DRV) (600 mg twice daily)	3300 (1255–7368)
Etravirine (ETR)	275 (81–2980)
Raltegravir (RAL)	72 (29–118)

Table 10. Identifying, Diagnosing, and Managing Acute HIV-1 Infection

- **Suspecting acute HIV infection:** Signs or symptoms of acute HIV infection with recent (within 2–6 weeks) high risk of exposure to HIV[a]
  - Signs/symptoms/laboratory findings may include but are not limited to one or more of the following: fever, lymphadenopathy, skin rash, myalgia/arthralgia, headache, diarrhea, oral ulcers, leucopenia, thrombocytopenia, transaminase elevation.
  - High-risk exposures include sexual contact with a person infected with HIV or at risk of HIV, sharing of injection drug use paraphernalia, or contact of potentially infectious blood with mucous membranes or breaks in skin.[a]
- **Differential diagnosis:** Epstein-Barr virus (EBV)- and non-EBV (e.g., cytomegalovirus [CMV])-related infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, syphilis
- **Evaluation/diagnosis of acute/primary HIV infection**
  - HIV antibody enzyme immunoassay (EIA) (rapid test if available)
    - Reactive EIA must be followed by Western blot.
    - Negative EIA or reactive EIA with negative or indeterminate Western blot should be followed by a virologic test.[b]
  - Positive virologic test[b] in this setting is consistent with acute HIV infection.
  - When acute HIV infection is diagnosed by a positive virologic test (such as HIV RNA or p24 antigen) that was preceded by a negative HIV antibody test, a confirmatory HIV antibody test should be performed over the next 3 months to confirm seroconversion.
- **Considerations for antiretroviral therapy:**
  - All pregnant women with acute or recent HIV infection should start on a combination ARV regimen as soon as possible because of the high risk of MTCT of HIV **(AI)**.
  - Treatment of acute and early HIV infection in nonpregnant persons is considered optional **(CIII)**.
  - Potentially unique benefits associated with ART during acute and early infection exist, although they remain unproven.
  - The risks of ART during acute and early infection are consistent with those for initiating ART in chronically infected asymptomatic patients with high CD4 counts.
  - If therapy is initiated, the goal should be for maintenance of maximal viral suppression.
  - Enrollment in a clinical trial should be considered.

[a] In some settings, behaviors conducive to acquisition of HIV infection might not be ascertained or might not be perceived as "high risk" by the health care provider or the patient or both. Thus, symptoms and signs consistent with acute retroviral syndrome should motivate consideration of this diagnosis even in the absence of reported high-risk behaviors.

[b] p24 antigen or HIV RNA assay. The p24 antigen is less sensitive but more specific than HIV RNA tests; HIV RNA tests are generally preferred. HIV RNA tests include quantitative branched DNA (bDNA), reverse transcriptase-polymerase chain reaction (RT-PCR), or qualitative transcription-mediated amplification (APTIMA, GenProbe).

Table 11. Drug Interactions between Antiretroviral Agents and Drugs Used to Treat Opioid Addiction (page 1 of 2)

Concomitant Drug	Antiretroviral Drug	Pharmacokinetic Interactions Clinical Comments/Recommendations
Buprenorphine	EFV	buprenorphine AUC ↓ 50%; norbuprenorphine[a] AUC ↓ 71% No withdrawal symptoms reported. No dosage adjustment recommended; however, monitor for withdrawal symptoms.
	ETR	buprenorphine AUC ↓ 25% No dosage adjustment necessary.
	ATV	buprenorphine AUC ↑ 93%; norbuprenorphine AUC ↑ 76%; ↓ ATV levels possible Do not coadminister buprenorphine with unboosted ATV.
	ATV/r	buprenorphine AUC ↑ 66%; norbuprenorphine AUC ↑ 105% Monitor for sedation. Buprenorphine dose reduction may be necessary.
	DRV/r	buprenorphine: no significant effect; norbuprenorphine AUC ↑ 46% and C_{min} ↑ 71% No dose adjustment necessary.
	FPV/r	buprenorphine: no significant effect; norbuprenorphine AUC ↓ 15% No dosage adjustment necessary.
	TPV/r	buprenorphine: no significant effect; norbuprenorphine AUC, C_{max}, and C_{min} ↓ 80%; TPV C_{min} ↓ 19%–40% Consider monitoring TPV level.
	3TC, ddI, TDF, ZDV, NVP, LPV/r, NFV	No significant effect No dosage adjustment necessary.
	ABC, d4T, FTC, ETR, IDV +/- RTV, SQV/r, RAL, MVC, T20	No data
Methadone	ABC	methadone clearance ↑ 22% No dosage adjustment necessary.
	d4T	d4T AUC ↓ 23% and C_{max} ↓ 44% No dosage adjustment necessary.
	ZDV	ZDV AUC ↑ 29%–43% Monitor for ZDV-related adverse effects.
	EFV	methadone AUC ↓ 52% Opioid withdrawal common; increased methadone dose often necessary.

Table 11. Drug Interactions between Antiretroviral Agents and Drugs Used to Treat Opioid Addiction (page 2 of 2)

Methadone, cont'd	NVP	methadone AUC ↓ 41% NVP: no significant effect Opioid withdrawal common; increased methadone dose often necessary.
	ATV/r, DRV/r, FPV/r, IDV/r, LPV/r, SQV/r, TPV/r	With ATV/r, DRV/r, FPV/r: R-methadone[b] AUC ↓ 16%–18%; With LPV/r: methadone AUC ↓ 26%–53%; With SQV/r 1000/100 mg BID: R-methadone AUC ↓ 19%; With TPV/r: R-methadone AUC ↓ 48% Opioid withdrawal unlikely but may occur. Adjustment of methadone dose usually not required; however, monitor for opioid withdrawal and increase methadone dose as clinically indicated.
	FPV	No data with FPV (unboosted) With APV: R-methadone C_{min} ↓ 21%, no significant change in AUC Monitor and titrate methadone as clinically indicated. The interaction with FPV is presumed to be similar.
	NFV	methadone AUC ↓ 40% Opioid withdrawal rarely occurs. Monitor and titrate dose as clinically indicated. May require increased methadone dose.
	ddI (EC capsule), 3TC, TDF, ETR, RTV, ATV, IDV, RAL	No significant effect No dosage adjustment necessary.
	FTC, MVC, T20	No data

[a] Norbuprenorphine is an active metabolite of buprenorphine.
[b] R-methadone is the active form of methadone.

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, APV = amprenavir, ATV = atazanavir, ATV/r = atazanavir/ ritonavair, AUC = area under the curve, BID = twice daily, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, d4T = stavudine, ddI = didanosine, DRV/r = darunavir/ritonavir, EC = enteric coated, EFV = efavirenz, ETR = etravirine, FPV = fosamprenavir, FPV/r = fosamprenavir/ritonavir, FTC = emtricitabine, IDV = indinavir, IDV/r = indinavir/ritonavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NVP = nevirapine, RAL = raltegravir, RTV = ritonavir, SQV/r = sacquinavir/ritonavir, T20 = enfuvirtide, TDF = tenofovir, TPV = tipranavir, TPV/r = tipranavir/ritonavir, ZDV = zidovudine

Table 12. Strategies to Improve Adherence to Antiretroviral Therapy

Strategies	Examples
Use a multidisciplinary team approach Provide an accessible, trusting health care team	• Nurses, social workers, pharmacists, and medications managers
Establish a trusting relationship with the patient	
Establish patient readiness to start ART	
Assess and simplify the regimen, if possible	
Identify potential barriers to adherence before starting ART	• Psychosocial issues • Active substance abuse or at high risk of relapse • Low literacy • Low numeracy • Busy daily schedule and/or travel away from home • Nondisclosure of HIV diagnosis • Skepticism about ART • Lack of prescription drug coverage • Lack of continuous access to medications
Provide resources for the patient	• Referrals for mental health and/or substance abuse treatment • Resources to obtain prescription drug coverage • Pillboxes
Involve the patient in ARV regimen selection	• For each option, review regimen potency, potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of nonadherence
Assess adherence at every clinic visit	• Use a simple checklist that the patient can complete in the waiting room • Ensure that other members of the health care team also assess adherence • Ask the patient open-ended questions (e.g., *In the last 3 days, please tell me how you took your medicines.*)
Identify the type of nonadherence	• Failure to fill the prescription(s) • Failure to take the right dose(s) at the right time(s) • Nonadherence to food requirements
Identify reasons for nonadherence	• Adverse effects from medications • Complexity of regimen (pill burden, dosing frequency, etc.) • Difficulty swallowing large pills • Forgetfulness • Failure to understand dosing instructions • Inadequate understanding of drug resistance and its relationship to adherence • Pill fatigue • Other potential barriers
If resources allow, select from among available effective interventions	• See http://www.cdc.gov/hiv/topics/research/prs/ma-good-evidence-interventions.htm

Key to Abbreviations: ART = antiretroviral therapy; ARV = antiretroviral

Table 13. Antiretroviral Therapy-Associated Common and/or Severe Adverse Effects
(See Appendix B for additional information listed by drug.) (Page 1 of 4)

Adverse Effects	NRTIs	NNRTIs	PIs	INSTI	EI
Bleeding events			**All PIs:** ↑ spontaneous bleeding, hematuria in patients with hemophilia **TPV:** Reports of intracranial hemorrhage. Risks include CNS lesions, trauma, surgery, hypertension, alcohol abuse, coagulopathy, and concomitant use of anti-coagulant or anti-platelet agents including vitamin E		
Bone marrow suppression	**ZDV:** Anemia, neutropenia				
Cardiovascular disease (CVD)	**ABC and ddI:** Associated with MI in some but not all cohort studies. Absolute risk greatest among patients with traditional CVD risk factors.		**PIs:** Associated with MI and stroke in some cohort studies. Data on newer PIs (ATV, DRV, and TPV) are limited. **SQV/r, ATV/r, and LPV/r:** PR interval prolongation. Risks include structural heart disease, conduction system abnormalities, cardiomyopathy, ischemic heart disease, and coadministration with drugs that prolong PR interval. **SQV/r:** QT interval prolongation in a healthy volunteer study. Risks include underlying heart conditions, pre-existing prolonged QT or arrhythmia, or use with other QT-prolonging drugs. ECG prior to SQV initiation is recommended and should be considered during therapy.		
Central nervous system (CNS) effects	**d4T:** Associated with rapidly progressive ascending neuromuscular weakness resembling Guillain-Barré syndrome (rare)	**EFV:** Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, suicidal ideation. Symptoms usually subside or diminish after 2–4 weeks. Bedtime dosing may reduce symptoms. Risks include history of psychiatric illness, concomitant use of agents with neuropsychiatric effects, and increased plasma EFV concentrations due to genetic factors or increased absorption with food.			

Table 13. Antiretroviral Therapy-Associated Common and/or Severe Adverse Effects
(See Appendix B for additional information listed by drug.) (Page 2 of 4)

Adverse Effects	NRTIs	NNRTIs	PIs	INSTI	EI
Diabetes mellitus (DM)/insulin resistance	**ZDV, d4T, and ddI**		• Reported for some **PIs (IDV, LPV/r)**, but not all PIs studied • **ATV +/- RTV** not found to alter insulin sensitivity of HIV-uninfected individuals in short-term studies.		
Dyslipidemia	**d4T > ZDV > ABC:** • ↑ LDL and TG	**EFV** • ↑ TG • ↑ LDL • ↑ HDL	**↑ LDL, ↑ TG, ↑ HDL: all RTV-boosted PIs** **↑ TG:** **LPV/r = FPV/r and LPV/r > DRV/r and ATV/r**		
Gastrointestinal (GI) effects	**Nausea and vomiting:** **ddI and ZDV > other NRTIs** **Pancreatitis: ddI**		GI intolerance (diarrhea, nausea, vomiting) **Diarrhea:** common with **NFV**. **LPV/r** > **DRV/r** and **ATV/r**		
Hepatic effects	Reported for most **NRTIs** **ddI:** Prolonged exposure linked to noncirrhotic portal hypertension, some cases with esophageal varicees **Steatosis:** Most commonly seen with **ZDV**, **d4T**, or **ddI** **Flares:** HIV/HBV-coinfected patients may develop severe hepatic flare when **TDF**, **3TC**, and **FTC** are withdrawn or when HBV resistance develops.	**NVP > other NNRTIs** **NVP:** • Severe hepatic toxicity with **NVP** is often associated with skin rash or symptoms of hypersensitivity. • For ARV-naive patients, risk is greater for women with pre-**NVP** CD4 count >250 cells/mm^3 and men with pre-**NVP** CD4 count >400 cells/mm^3. Overall risk is higher for women than men. • Risk is greatest in the first few months of treatment. • 2-week dose escalation of **NVP** reduces risk of rash and possibly hepatotoxicity if related to hypersensitivity. • **NVP** is contraindicated in patients with Child-Pugh classification B or C. • Liver failure observed in HIV-uninfected individuals receiving **NVP** for post-exposure prophylaxis. **NVP** should never be used for this indication.	**All PIs:** Drug-induced hepatitis and hepatic decompensation (and rare cases of fatalities) have been reported with all PIs to varying degrees. The frequency of hepatic events is higher with TPV/r than with other PIs. **IDV, ATV:** Jaundice due to indirect hyperbilirubinemia **TPV/r:** Contraindicated in patients with moderate to severe hepatic insufficiency (Child-Pugh classification B or C)		**MVC:** Hepatotoxicity with or without rash or HSRs reported

Table 13. Antiretroviral Therapy-Associated Common and/or Severe Adverse Effects
(See Appendix B for additional information listed by drug.) (Page 3 of 4)

Adverse Effects	NRTIs	NNRTIs	PIs	INSTI	EI
Hypersensitivity reaction (HSR) (excluding rash alone or Stevens Johnson syndrome[SJS])	**ABC:** • HLA-B*5701 screening should be performed prior to initiation of **ABC** and **ABC** should not be started if HLA-B*5701 is positive. • Symptoms of HSR include (in descending frequency): fever, skin rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms. • Symptoms worsen with continuation of **ABC** • Median onset of reactions is 9 days; ~ 90% of reactions within first 6 weeks • Onset of rechallenge reactions is within hours of rechallenge dose • Patients, regardless of HLA-B*5701 status, should not be rechallenged with **ABC** if HSR suspected.	**NVP:** • Hypersensitivity syndrome of hepatic toxicity and rash that may be accompanied by fever, general malaise, fatigue, myalgias, arthralgias, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, granulocytopenia, lymphadenopathy, or renal dysfunction. • In ARV-naive patients, risk is greater for women with pre-**NVP** CD4 count >250 cells/mm^3 and men with pre-**NVP** CD4 count >400 cells/mm^3. Overall, risk is higher for women than men. • 2-week dose escalation of **NVP** reduces risk.		**RAL**	**MVC:** reported as part of a syndrome related to hepatotoxicity
Lactic acidosis	**NRTIs**, especially **d4T**, **ZDV**, and **ddI** • Insidious onset with GI prodrome, weight loss, and fatigue. May be rapidly progressive, with tachycardia, tachypnea, jaundice, muscular weakness, mental status changes, respiratory distress, pancreatitis, and organ failure. • Mortality up to 50% in some case series, especially in patients with serum lactate >10 mmol/L • Females and obese patients at increased risk. **Laboratory findings:** • ↑ lactate (often >5 mmol/L), anion gap, AST, ALT, PT, bilirubin • ↑ amylase and lipase in patients with pancreatitis • ↓ arterial pH, serum bicarbonate, serum albumin				

Table 13. Antiretroviral Therapy-Associated Common and/or Severe Adverse Effects
(See Appendix B for additional information listed by drug.) (Page 4 of 4)

Adverse Effects	NRTIs	NNRTIs	PIs	INSTI	EI
Lipodystrophy	**Lipoatrophy: Thymidine analogs** (**d4T** > **ZDV**). May be more likely when combined with **EFV** than with a ritonavir-boosted **PI**.	**Lipohypertophy:** Trunk fat increase observed with **EFV**-, **PI**-, and **RAL**-containing regimens; however, causal relationship has not been established.			
Myopathy/elevated creatine phosphokinase (CPK)	**ZDV:** myopathy			**RAL:** ↑ CPK. muscle weakness and rhabdomyolysis	
Nephrotoxicity/ urolithiasis	**TDF:** ↑ serum creatinine, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, non-anion gap metabolic acidosis Concurrent use of **PI** may increase risk.		**IDV:** ↑ serum creatinine, pyuria; hydronephrosis or renal atrophy **IDV, ATV:** Stone, crystal formation; adequate hydration may reduce risk.		
Osteopenia/ osteoporosis	**TDF:** Associated with greater loss of BMD than ZDV, d4T, and ABC.	Decreases in BMD observed in studies of regimens containing different **NRTIs** combined with either **NNRTIs** or **PIs**.			
Peripheral neuropathy	**Peripheral neuropathy** (pain and/or paresthesias, lower extremities > upper extremities): **d4T** > **ddI** and **ddC** (can be irreversible)				
Rash		**All NNRTIs**	**ATV, DRV, FPV**	**RAL:** Uncommon	**MVC**
Stevens-Johnson syndrome (SJS)/ toxic epidermal necrosis (TEN)	**ddI, ZDV:** Reported cases	**NVP > DLV, EFV, ETR, RPV**	**FPV, DRV, IDV, LPV/r, ATV:** Reported cases	**RAL**	

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ALT = alanine aminotransferase, ARV = antiretroviral, AST = aspartate aminotransferase, ATV = atazanavir, ATV/r = atazanavir + ritonavir, BMD = bone mineral density, CNS = central nervous system, CPK = creatine phosphokinase, CVD = cardiovascular disease, d4T = stavudine, ddC = zalcitabine, ddI = didanosine, DLV = delaviridine, DM = diabetes mellitus, DRV = darunavir, DRV/r = darunavir + ritonavir, ECG = electrocardiogram, EFV = efavirenz, EI = entry inhibitor, ETR = etravirine, FPV = fosamprenavir, FPV/r = fosamprenavir + ritonavir, FTC = emtricitabine, GI = gastrointestinal, HBV = hepatitis B virus, HDL = high-density lipoprotein, HSR = hypersensitivity reaction, IDV = indinavir, INSTI = integrase strand transfer inhibitor, LDL = low-density lipoprotein, LPV/r = lopinavir + ritonavir, MI = myocardial infarction, MVC = maraviroc, NFV = nelfinavir, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PI = protease inhibitor, PT = prothrombin time, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SJS = Stevens-Johnson syndrome, SQV = saquinavir, SQV/r = saquinavir + ritonavir, TDF = tenofovir, TEN = toxic epidermal necrosis, TG = triglyceride, TPV = tipranavir, TPV/r = tipranavir + ritonavir, ZDV = zidovudine

Table 14. Drugs That Should Not Be Used With Protease Inhibitors, Non-Nucleoside Reverse Transcriptase Inhibitors, or CCR5 Antagonist (page 1 of 2)

This table lists only drugs that should not be coadministered at any dose and regardless of RTV boosting. See Tables 15 and 16 for more detailed PK interaction data.

Drug Categories										
Antiretroviral Agents[a,b]	**Cardiac Agents**	**Lipid-Lowering Agents**	**Antimyco-bacterials**	**Gastro-intestinal Drugs**	**Neuro-leptics**	**Psycho-tropics**	**Ergot Derivatives (vasoconstrictors)**	**Herbs**	**Antiretroviral Agents**	**Others**
ATV +/– RTV	none	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	ETR NVP	alfuzosin irinotecan salmeterol sildenafil for PAH
DRV/r	none	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	none	alfuzosin salmeterol sildenafil for PAH
FPV +/– RTV	flecainide propafenone	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	ETR	alfuzosin salmeterol sildenafil for PAH
LPV/r	none	lovastatin simvastatin	rifampin[d] rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	none	alfuzosin salmeterol sildenafil for PAH
SQV/r	amiodarone dofetilide flecainide lidocaine propafenone quinidine	lovastatin simvastatin	rifampin[d] rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam trazodone	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort garlic supple-ments	none	alfuzosin salmeterol sildenafil for PAH
TPV/r	amiodarone flecainide propafenone quinidine	lovastatin simvastatin	rifampin rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	ETR	alfuzosin salmeterol sildenafil for PAH
EFV	none	none	rifapentine[c]	cisapride[e]	pimozide	midazolam[f] triazolam	dihydroergotamine ergonovine ergotamine methylergonovine	St. John's wort	other NNRTIs	none
ETR	none	none	rifampin rifapentine[c]	none	none	none	none	St John's wort	unboosted PIs ATV/r, FPV/r, or TPV/r other NNRTIs	carbamazepine phenobarbital phenytoin clopidogrel
NVP	none	none	rifapentine[c]	none	none	none	none	St. John's wort	ATV +/– RTV other NNRTIs	ketoconazole
RPV	none	none	rifabutin rifampin rifapentine[c]	proton pump inhibitors	none	none	none	St. John's wort	other NNRTIs	carbamazepine oxcarbazepine phenobarbital phenytoin
MVC	none	none	rifapentine[c]	none	none	none	none	St. John's wort	none	none

Table 14. Drugs That Should Not Be Used With Protease Inhibitors, Non-Nucleoside Reverse Transcriptase Inhibitors, or CCR5 Antagonist (page 2 of 2)

[a] DLV, IDV, NFV, and RTV (as sole PI) are not included in this table. Refer to the FDA package insert for information regarding DLV-, IDV-, NFV-, and RTV (as sole PI)-related drug interactions.

[b] Certain listed drugs are contraindicated on the basis of theoretical considerations. Thus, drugs with narrow therapeutic indices and suspected metabolic involvement with CYP450 3A, 2D6, or unknown pathways are included in this table. Actual interactions may or may not occur in patients.

[c] HIV-infected patients treated with rifapentine have a higher rate of TB relapse than those treated with other rifamycin-based regimens. Therefore an alternative agent to rifapentine is recommended.

[d] A high rate of Grade 4 serum transaminase elevation was seen when a higher dose of RTV was added to LPV/r or SQV or when double-dose LPV/r was used with rifampin to compensate for rifampin's induction effect, so these dosing strategies should not be used.

[e] The manufacturer of cisapride has a limited-access protocol for patients who meet specific clinical eligibility criteria.

[f] Use of oral midazolam is contraindicated. Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.

Suggested alternatives to:

Lovastatin, simvastatin: Fluvastatin, pitavastatin, and pravastatin have the least potential for drug-drug interactions (except for pravastatin with DRV/r, see Table 15a). Use atorvastatin and rosuvastatin with caution; start with the lowest possible dose and titrate based on tolerance and lipid-lowering efficacy.

Rifampin: Rifabutin (with dosage adjustment, see Tables 15a and 15b)

Midazolam, triazolam: temazepam, lorazepam, oxazepam

Key to Abbreviations: ATV +/- RTV = atazanavir +/- ritonavir, ATV/r = atazanavir/ritonavir, CYP = cytochrome P, DLV = delavirdine, DRV/r = darunavir/ritonavir, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, FPV +/- RTV = fosamprenavir +/- ritonavir, FPV/r = fosamprenavir/ritonavir, IDV = indinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PAH = pulmonary arterial hypertension, PI = protease inhibitor, PK = pharmacokinetic, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir/ritonavir, TB = tuberculosis, TPV/r = tipranavir/ritonavir

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 1 of 11)*

This table provides information relating to PK interactions between PIs and non-ARV drugs. When information is available, interactions with boosted and unboosted PIs are listed separately. For interactions among ARV agents and for dosing recommendations, refer to Table 16a.

* NFV and IDV are not included in this table. Please refer to the NFV and IDV FDA package inserts for information regarding drug interactions with these PIs.

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV +/– RTV	When given simultaneously, ↓ ATV expected	Give ATV at least 2 hours before or 1 hour after antacids or buffered medications.
	FPV	APV AUC ↓ 18%; no significant change in APV C_{min}	Give FPV simultaneously with or at least 2 hours before or 1 hour after antacids.
	TPV/r	TPV AUC ↓ 27%	Give TPV at least 2 hours before or 1 hour after antacids.
H2 Receptor Antagonists	**RTV-boosted PIs**		
	ATV/r	↓ ATV	H2 receptor antagonist dose should not exceed a dose equivalent to famotidine 40 mg BID in ART-naive patients or 20 mg BID in ART-experienced patients. Give ATV 300 mg + RTV 100 mg simultaneously with and/or ≥10 hours after the H2 receptor antagonist. If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV 400 mg + RTV 100 mg.
	DRV/r, LPV/r	No significant effect	No dosage adjustment necessary.
	PIs without RTV		
	ATV	↓ ATV	H2 receptor antagonist single dose should not exceed a dose equivalent of famotidine 20 mg or total daily dose equivalent of famotidine 20 mg BID in ART-naive patients. Give ATV at least 2 hours before and at least 10 hours after the H2 receptor antagonist.
	FPV	APV AUC ↓ 30%; no significant change in APV C_{min}	Give FPV at least 2 hours before H2 receptor antagonist if concomitant use is necessary. Consider boosting with RTV.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 2 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Proton Pump Inhibitors (PPIs)	ATV	↓ ATV	**PPIs are not recommended in patients receiving unboosted ATV.** In these patients, consider alternative acid-reducing agents, RTV boosting, or alternative PIs.
	ATV/r	↓ ATV	PPIs should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/r. **PPIs are not recommended in PI-experienced patients.**
	DRV/r, TPV/r	↓ omeprazole PI: no significant effect	May need to increase omeprazole dose when using TPV/r.
	FPV +/- RTV, LPV/r	No significant effect	No dosage adjustment necessary.
	SQV/r	SQV AUC ↑ 82%	Monitor for SQV toxicities.
Anticoagulants			
Warfarin	ATV +/- RTV, DRV/r, FPV +/- RTV, LPV/r, SQV/r, TPV/r	↑ or ↓ warfarin possible DRV/r ↓ S-warfarin AUC 21%	Monitor INR closely when stopping or starting PI and adjust warfarin dose accordingly.
Anticonvulsants			
Carbamazepine	**RTV-boosted PIs**		
	ATV/r, FPV/r, LPV/r, SQV/r, TPV/r	↑ carbamazepine possible TPV/r ↑ carbamazepine AUC 26% May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r once daily.**
	DRV/r	carbamazepine AUC ↑ 45% DRV: no significant change	Monitor anticonvulsant level and adjust dose accordingly.
	PIs without RTV		
	ATV, FPV	May ↓ PI levels substantially	Monitor anticonvulsant level and virologic response. Consider alternative anticonvulsant, RTV boosting for ATV and FPV, and/or monitoring PI level.
Lamotrigine	LPV/r	lamotrigine AUC ↓ 50% LPV: no significant change	Titrate lamotrigine dose to effect or consider alternative anticonvulsant. A similar interaction is possible with other RTV-boosted PIs.
Phenobarbital	All PIs	May ↓ PI levels substantially	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r once daily.**

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 3 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Phenytoin	**RTV-boosted PIs**		
	ATV/r, DRV/r, SQV/r, TPV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response.
	FPV/r	phenytoin AUC ↓ 22% APV AUC ↑ 20%	Monitor phenytoin level and adjust dose accordingly. No change in FPV/r dose recommended.
	LPV/r	phenytoin AUC ↓ 31% LPV/r AUC ↓ 33%	Consider alternative anticonvulsant or monitor levels of both drugs and assess virologic response. **Do not coadminister with LPV/r once daily.**
	PIs without RTV		
	ATV, FPV	May ↓ PI levels substantially	Consider alternative anticonvulsant, RTV boosting for ATV and FPV, and/or monitoring PI level. Monitor anticonvulsant level and virologic response.
Valproic Acid (VPA)	LPV/r	↓VPA possible LPV AUC ↑ 75%	Monitor VPA levels and virologic response. Monitor for LPV-related toxicities.
Antidepressants			
Bupropion	LPV/r	bupropion AUC ↓ 57%	Titrate bupropion dose based on clinical response.
	TPV/r	bupropion AUC ↓ 46%	
Paroxetine	DRV/r	paroxetine AUC ↓ 39%	Titrate paroxetine dose based on clinical response.
	FPV/r	paroxetine AUC ↓ 55%	
Sertraline	DRV/r	sertraline AUC ↓ 49%	Titrate sertraline dose based on clinical response.
Trazodone	ATV +/- RTV, DRV/r, FPV +/- RTV, LPV/r, TPV/r	RTV 200 mg BID (for 2 days) ↑ trazodone AUC 240%	Use lowest dose of trazodone and monitor for CNS and cardiovascular adverse effects.
	SQV/r	↑ trazodone expected	**Contraindicated. Do not coadminister.**
Tricyclic Antidepressants (TCAs) (Amitriptyline, Desipramine, Imipramine, Nortriptyline)	All RTV-boosted PIs	↑ TCA expected	Use lowest possible TCA dose and titrate based on clinical assessment and/or drug levels.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 4 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals			
Fluconazole	**RTV-boosted PIs**		
	ATV/r	No significant effect	No dosage adjustment necessary.
	SQV/r	No data with RTV boosting SQV (1200 mg TID) AUC ↑ 50%	No dosage adjustment necessary.
	TPV/r	TPV AUC ↑ 50%	Fluconazole >200 mg daily is not recommended. If high-dose fluconazole is indicated, consider alternative PI or another class of ARV drug.
Itraconazole	**RTV-boosted PIs**		
	ATV/r, DRV/r, FPV/r, TPV/r	↑ itraconazole possible ↑ PI possible	Consider monitoring itraconazole level to guide dosage adjustments. High doses (>200 mg/day) are not recommended unless dose is guided by itraconazole levels.
	LPV/r	↑ itraconazole	Consider not exceeding 200 mg itraconazole daily or monitor itraconazole level.
	SQV/r	Bidirectional interaction has been observed	Dose not established, but decreased itraconazole dosage may be warranted. Consider monitoring itraconazole level.
	PIs without RTV		
	ATV, FPV	↑ itraconazole possible ↑ PI possible	Consider monitoring itraconazole level to guide dosage adjustments.
Posaconazole	ATV/r	ATV AUC ↑ 146%	Monitor for adverse effects of ATV.
	ATV	ATV AUC ↑ 268%	Monitor for adverse effects of ATV.
Voriconazole	**RTV-boosted PIs**		
	ATV/r, DRV/r, FPV/r, LPV/r, SQV/r, TPV/r	RTV 400 mg BID ↓ voriconazole AUC 82% RTV 100 mg BID ↓ voriconazole AUC 39%	**Do not coadminister** voriconazole and RTV unless benefit outweighs risk. If administered, consider monitoring voriconazole level and adjust dose accordingly.
	PIs without RTV		
	ATV, FPV	↑ voriconazole possible ↑ PI possible	Monitor for toxicities.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 5 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anti-mycobacterials			
Clarithromycin	ATV +/– RTV	clarithromycin AUC ↑ 94%	May cause QTc prolongation. Reduce clarithromycin dose by 50%. Consider alternative therapy (e.g., azithromycin).
	DRV/r, FPV/r, LPV/r, SQV/r, TPV/r	DRV/r ↑ clarithromycin AUC 57% FPV/r ↑ clarithromycin possible LPV/r ↑ clarithromycin expected RTV 500 mg BID ↑ clarithromycin 77% SQV unboosted ↑ clarithromycin 45% TPV/r ↑ clarithromycin 19% clarithromycin ↑ unboosted SQV 177% clarithromycin ↑ TPV 66%	Monitor for clarithromycin-related toxicities or consider alternative macrolide (e.g., azithromycin). Reduce clarithromycin dose by 50% in patients with CrCl 30–60 mL/min. Reduce clarithromycin dose by 75% in patients with CrCl <30 mL/min.
	FPV	APV AUC ↑ 18%	No dosage adjustment necessary.
Rifabutin	**RTV-boosted PIs**		
	ATV/r	rifabutin (150 mg once daily) AUC ↑ 110% and metabolite AUC ↑ 2101% compared with rifabutin (300 mg daily) administered alone	Rifabutin 150 mg once daily or 300 mg three times a week. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. PK data reported in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in HIV-infected patients than in the healthy study participants.
	DRV/r	rifabutin (150 mg every other day) AUC not significantly changed and metabolite AUC ↑ 881% compared with rifabutin (300 mg once daily) administered alone	
	FPV/r	rifabutin (150 mg every other day) and metabolite AUC ↑ 64% compared with rifabutin (300 mg once daily) administered alone	
	LPV/r	rifabutin (150 mg once daily) and metabolite AUC ↑ 473% compared with rifabutin (300 mg daily) administered alone	
	SQV/r	↑ rifabutin with unboosted SQV	
	TPV/r	rifabutin (150 mg x 1 dose) and metabolite AUC ↑ 333%	
	PIs without RTV		
	ATV, FPV	↑ rifabutin AUC expected	Rifabutin 150 mg daily or 300 mg three times a week

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 6 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifampin	All PIs	↓ PI >75% approximately	**Do not coadminister rifampin and PIs.** Additional RTV does not overcome this interaction and increases hepatotoxicity.
Rifapentine	All PIs	↓ PI expected	**Do not coadminister rifapentine and PIs.**
Benzodiazepines			
Alprazolam **Diazepam**	All PIs	↑ benzodiazepine possible RTV (200 mg BID for 2 days) ↑ alprazolam half-life 222% and AUC 248%	Consider alternative benzodiazepines such as lorazepam, oxazepam, or temazepam.
Lorazepam **Oxazepam** **Temazepam**	All PIs	No data	These benzodiazepines metabolized via non-CYP450 pathways; less interaction potential compared with other benzodiazepines.
Midazolam	All PIs	↑ midazolam expected SQV/r ↑ midazolam (oral) AUC 1144% and C_{max} 327%	**Do not coadminister oral midazolam and PIs.** Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.
Triazolam	All PIs	↑ triazolam expected RTV (200 mg BID) ↑ triazolam half-life 1200% and AUC 2000%	**Do not coadminister triazolam and PIs.**
Cardiac Medications			
Bosentan	All PIs	LPV/r ↑ bosentan 48-fold (Day 4) and 5-fold (Day 10) ↓ ATV expected	**Do not coadminister bosentan and ATV without RTV.** In patients on a PI (other than unboosted ATV) >10 days: start bosentan at 62.5 mg once daily or every other day. In patients on bosentan who require a PI (other than unboosted ATV): stop bosentan >36 hours before PI initiation and restart 10 days after PI initiation at 62.5 mg once daily or every other day.
Digoxin	RTV, SQV/r	RTV (200 mg BID) ↑ digoxin AUC 29% and half-life 43% SQV/r ↑ digoxin AUC 49%	Use with caution. Monitor digoxin levels. Digoxin dose may need to be decreased.
Dihydropyridine Calcium Channel Blockers (CCBs)	All PIs	↑ dihydropyridine possible	Use with caution. Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB used with ATV.
Diltiazem	ATV +/– RTV	diltiazem AUC ↑ 125%	Decrease diltiazem dose by 50%. ECG monitoring is recommended.
	DRV/r, FPV +/– RTV, LPV/r, SQV/r, TPV/r	↑ diltiazem possible	Use with caution. Adjust diltiazem according to clinical response and toxicities.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 7 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Corticosteroids			
Dexamethasone	All PIs	↓ PI levels possible	Use systemic dexamethasone with caution or consider alternative corticosteroid for long-term use.
Fluticasone (inhaled or intranasal)	All RTV-boosted PIs	RTV 100 mg BID ↑ fluticasone AUC 350-fold and ↑ C_{max} 25-fold	Coadministration can result in adrenal insufficiency, including Cushing's syndrome. **Do not coadminister unless potential benefits of inhaled fluticasone outweigh the risks of systemic corticosteroid adverse effects.**
Prednisone	LPV/r	↑ prednisolone AUC 31%	No dosage adjustment necessary.
Hepatitis C NS3/4A Protease Inhibitors			
Boceprevir	ATV/r	ATV AUC ↓ 35%, C_{min} ↓ 49% RTV AUC ↓ 36% boceprevir AUC ↔	**Coadministration is not recommended.**
	DRV/r	DRV AUC ↓ 44%, C_{min} ↓ 59% RTV AUC ↓ 26% boceprevir AUC ↓ 29%, C_{min} ↓ 35%	**Coadministration is not recommended.**
	LPV/r	LPV AUC ↓ 34%, C_{min} ↓ 43% RTV AUC ↓ 23% boceprevir AUC ↓ 44%, C_{min} ↓ 35%	**Coadministration is not recommended.**
Telaprevir	ATV/r	telaprevir AUC ↓ 20%	No dose adjustment necessary.
	DRV/r	telaprevir AUC ↓ 35% DRV AUC ↓ 40%	**Coadministration is not recommended.**
	FPV/r	telaprevir AUC ↓ 32% APV AUC ↓ 47%	**Coadministration is not recommended.**
	LPV/r	telaprevir AUC ↓ 54% LPV: no significant change	**Coadministration is not recommended.**
Herbal Products			
St. John's Wort	All PIs	↓ PI expected	**Do not coadminister.**
Hormonal Contraceptives			
Hormonal Contraceptives	**RTV-boosted PIs**		
	ATV/r	ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% norgestimate ↑ 85%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol. Oral contraceptives containing progestins other than norethindrone or norgestimate have not been studied.[a]
	DRV/r	ethinyl estradiol AUC ↓ 44% norethindrone AUC ↓ 14%	Use alternative or additional contraceptive method.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 8 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Contraceptives	FPV/r	ethinyl estradiol AUC ↓ 37% norethindrone AUC ↓ 34%	Use alternative or additional contraceptive method.
	LPV/r	ethinyl estradiol AUC ↓ 42% norethindrone AUC ↓ 17%	Use alternative or additional contraceptive method.
	SQV/r	↓ ethinyl estradiol	Use alternative or additional contraceptive method.
	TPV/r	ethinyl estradiol AUC ↓ 48% norethindrone: no significant change	Use alternative or additional contraceptive method.
	PIs without RTV		
	ATV	ethinyl estradiol AUC ↑ 48% norethindrone AUC ↑ 110%	Use oral contraceptive that contains no more than 30 mcg of ethinyl estradiol or use alternative contraceptive method. Oral contraceptives containing less than 25 mcg of ethinyl estradiol or progestins other than norethindrone or norgestimate have not been studied.[b]
	FPV	With APV: ↑ ethinyl estradiol and ↑ norethindrone C_{min} ; APV C_{min} ↓ 20%	Use alternative method.
HMG-CoA Reductase Inhibitors			
Atorvastatin	ATV +/- RTV	↑ atorvastatin possible	Titrate atorvastatin dose carefully and use lowest dose necessary.
	DRV/r FPV +/- RTV SQV/r	DRV/r + atorvastatin 10 mg similar to atorvastatin 40 mg administered alone; FPV +/– RTV ↑ atorvastatin AUC 130%–153%; SQV/r ↑ atorvastatin AUC 79%	Titrate atorvastatin dose carefully and use the lowest necessary dose. Do not exceed 20 mg atorvastatin daily.
	LPV/r	LPV/r ↑ atorvastatin AUC 488%	Use with caution and use the lowest atorvastatin dose necessary.
	TPV/r	↑ atorvastatin AUC 836%	**Do not coadminister.**
Lovastatin	All PIs	Significant ↑ lovastatin expected	**Contraindicated. Do not coadminister.**
Pitavastatin	All PIs	ATV ↑ pitavastatin AUC 31% and C_{max} ↑ 60% ATV: no significant effect DRV ↓ pitavastatin AUC 26% DRV: no significant effect LPV/r ↓ pitavastatin AUC 20% LPV: no significant effect	No dose adjustment necessary.
Pravastatin	DRV/r	pravastatin AUC ↑ 81%	Use lowest possible starting dose with careful monitoring.
	LPV/r	pravastatin AUC ↑ 33%	No dose adjustment necessary.
	SQV/r	pravastatin AUC ↓ 47%–50%	No dose adjustment necessary.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 9 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rosuvastatin	ATV/r, LPV/r	ATV/r ↑ rosuvastatin AUC 213% and C_{max} ↑ 600% LPV/r ↑ rosuvastatin AUC 108% and C_{max} ↑ 366%	Titrate rosuvastatin dose carefully and use the lowest necessary dose. Do not exceed 10 mg rosuvastatin daily.
	DRV/r	rosuvastatin AUC ↑ 48% and C_{max} ↑ 139%	Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities.
	FPV +/- RTV	No significant effect on rosuvastatin	No dosage adjustment necessary
	SQV/r	No data available	Titrate rosuvastatin dose carefully and use the lowest necessary dose while monitoring for toxicities.
	TPV/r	rosuvastatin AUC ↑ 26% and C_{max} ↑ 123%	No dosage adjustment necessary.
Simvastatin	All PIs	Significant ↑ simvastatin level; SQV/r 400 mg/400 mg BID ↑ simvastatin AUC 3059%	**Contraindicated. Do not coadminister.**
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	ATV	buprenorphine AUC ↑ 93% norbuprenorphine[c] AUC ↑ 76% ↓ ATV possible	**Do not coadminister buprenorphine with unboosted ATV.**
	ATV/r	buprenorphine AUC ↑ 66% norbuprenorphine[c] AUC ↑ 105%	Monitor for sedation. Buprenorphine dose reduction may be necessary.
	DRV/r	buprenorphine: no significant effect norbuprenorphine[c] AUC ↑ 46% and C_{min} ↑ 71%	No dosage adjustment necessary. Clinical monitoring is recommended.
	FPV/r	buprenorphine: no significant effect norbuprenorphine[c] AUC ↓ 15%	No dosage adjustment necessary. Clinical monitoring is recommended.
	LPV/r	No significant effect	No dosage adjustment necessary
	TPV/r	buprenorphine: no significant effect norbuprenorphine[c] AUC, C_{max}, and C_{min} ↓ 80% TPV C_{min} ↓ 19%–40%	Consider monitoring TPV level.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 10 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Methadone	**RTV-boosted PIs**		
	ATV/r, DRV/r, FPV/r, LPV/r, SQV/r, TPV/r	ATV/r, DRV/r, FPV/r ↓ R-methadone[d] AUC 16%–18%; LPV/r ↓ methadone AUC 26%–53%; SQV/r 1000/100 mg BID ↓ R-methadone[d] AUC 19%; TPV/r ↓ R-methadone[d] AUC 48%	Opioid withdrawal unlikely but may occur. No adjustment in methadone usually required but monitor for opioid withdrawal and increase methadone dose as clinically indicated.
	PIs without RTV		
	ATV	No significant effect	No dosage adjustment necessary.
	FPV	No data with unboosted FPV APV ↓ R-methadone[d] C_{min} 21%, AUC no significant change	Monitor and titrate methadone as clinically indicated. The interaction with FPV is presumed to be similar.
Phosphodiesterase Type 5 (PDE5) Inhibitors			
Sildenafil	All PIs	DRV/r + sildenafil 25 mg similar to sildenafil 100 mg alone; RTV 500 mg BID ↑ sildenafil AUC 1000%; SQV unboosted ↑ sildenafil AUC 210%	For treatment of erectile dysfunction Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil. For treatment of PAH **Contraindicated**
Tadalafil	All PIs	RTV 200 mg BID ↑ tadalafil AUC 124%; TPV/r (1st dose) ↑ tadalafil AUC 133%; TPV/r steady state: no significant effect	For treatment of erectile dysfunction Start with tadalafil 5-mg dose and do not exceed a single dose of 10 mg every 72 hours. Monitor for adverse effects of tadalafil. For treatment of PAH *In patients on a PI >7 days:* Start with tadalafil 20 mg once daily and increase to 40 mg once daily based on tolerability. *In patients on tadalafil who require a PI:* Stop tadalafil >24 hours prior to PI initiation, restart 7 days after PI initiation at 20 mg once daily, and increase to 40 mg once daily based on tolerability. For treatment of benign prostatic hyperplasia Maximum recommended daily dose is 2.5 mg per day
Vardenafil	All PIs	RTV 600 mg BID ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil.

Table 15a. Drug Interactions between Protease Inhibitors and Other Drugs (Page 11 of 11)*

Concomitant Drug	PI	Effect on PI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous Interactions			
Colchicine	All PIs	RTV 100 mg BID ↑ colchicine AUC 296%, C_{max} 184% With all PIs: significant ↑ in colchicine AUC expected	For treatment of gout flares Colchicine 0.6 mg x 1 dose, followed by 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. *With FPV without RTV:* 1.2 mg x 1 dose and no repeat dose for at least 3 days For prophylaxis of gout flares Colchicine 0.3 mg once daily or every other day *With FPV without RTV:* colchicine 0.3 mg BID or 0.6 mg once daily or 0.3 mg once daily For treatment of familial Mediterranean fever Do not exceed colchicine 0.6 mg once daily or 0.3 mg BID. *With FPV without RTV:* Do not exceed 1.2 mg once daily or 0.6 mg BID. **Do not coadminister in patients with hepatic or renal impairment.**
Salmeterol	All PIs	↑ salmeterol possible	**Do not coadminister** because of potential increased risk of salmeterol-associated cardiovascular events, including QT prolongation, palpitations, and sinus tachycardia.
Atovaquone/ proguanil	ATV/r, LPV/r	ATV/r ↓ atovaquone AUC 46% and ↓ proguanil AUC 41% LPV/r ↓ atovaquone AUC 74% and ↓ proguanil AUC 38%	No dosage recommendation. Consider alternative drug for malaria prophylaxis, if possible.

[a] The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate (generic formulation may also be available): Ovcon 35, 50; Femcon Fe; Brevicon; Modicon; Ortho-Novum 1/35, 10/11, 7/7/7; Norinyl 1/35; Tri-Norinyl; Ortho-Cyclen; Ortho Tri-Cyclen.

[b] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate (generic formulation may also be available): Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Ortho Tri-Cyclen Lo.

[c] Norbuprenorphine is an active metabolite of buprenorphine.

[d] R-methadone is the active form of methadone.

Key to Abbreviations: APV = amprenavir, ART = antiretroviral therapy, ARV = antiretroviral, ATV = atazanavir, ATV/r = atazanavir + ritonavir, AUC = area under the curve, BID = twice daily, CCB = calcium channel blocker, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, CNS = central nervous system, CrCl = creatinine clearance, CYP = cytochrome P, DRV = darunavir, DRV/r = darunavir + ritonavir, ECG = electrocardiogram, FDA = Food and Drug Administration, FPV = fosamprenavir (FPV is a prodrug of APV), FPV/r = fosamprenavir + ritonavir, IDV = indinavir, INR = international normalized ratio, LPV = lopinavir, LPV/r = lopinavir + ritonavir, NFV = nelfinavir, PAH = pulmonary arterial hypertension, PDE5 = phosphodiesterase type 5, PI = protease inhibitor, PK = pharmacokinetic, PPI = proton pump inhibitor, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinavir + ritonavir, TCA = tricyclic antidepressant, TDF = tenofovir, TID = three times a day, TPV = tipranavir, TPV/r = tipranavir + ritonavir, VPA = valproic acid

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Page 1 of 6)*

This table provides information relating to PK interactions between NNRTIs and non-ARV drugs. For interactions among ARV agents and for dosing recommendations, refer to Table 16b.

*DLV is not included in this table. Please refer to the DLV FDA package insert for information regarding DLV drug interactions.

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	RPV	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	RPV	↓ RPV	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
Proton Pump Inhibitors (PPI)	RPV	↓ RPV	**Contraindicated. Do not coadminister.**
Anticoagulants/Antiplatelets			
Warfarin	EFV, NVP	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
	ETR	↑ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Clopidogrel	ETR	↓ activation of clopidogrel possible	ETR may prevent metabolism of clopidogrel (inactive) to its active metabolite. Avoid coadministration, if possible.
Anticonvulsants			
Carbamazepine Phenobarbital Phenytoin	EFV	carbamazepine + EFV: carbamazepine AUC ↓ 27% and EFV AUC ↓ 36% phenytoin + EFV: ↓ EFV and ↓ phenytoin possible	Monitor anticonvulsant and EFV levels or, if possible, use alternative anticonvulsant to those listed.
	ETR	↓ anticonvulsant and ETR possible	**Do not coadminister.** Consider alternative anticonvulsant.
	NVP	↓ anticonvulsant and NVP possible	Monitor anticonvulsant and NVP levels and virologic responses or consider alternative anticonvulsant.
	RPV	↓ RPV possible	**Contraindicated. Do not coadminister.** Consider alternative anticonvulsant.
Antidepressants			
Bupropion	EFV	bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
Paroxetine	EFV, ETR	No significant effect	No dosage adjustment necessary.
Sertraline	EFV	sertraline AUC ↓ 39%	Titrate sertraline dose based on clinical response.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Page 2 of 6)*

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antifungals			
Fluconazole	EFV	No significant effect	No dosage adjustment necessary.
	ETR	ETR AUC ↑ 86%	No dosage adjustment necessary. Use with caution.
	NVP	NVP AUC ↑ 110%	Increased risk of hepatotoxicity possible with this combination. Monitor NVP toxicity or use alternative ARV agent.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection. (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with fluconazole.)
Itraconazole	EFV	itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 35%–44%	Failure to achieve therapeutic itraconazole concentrations has been reported. Avoid this combination if possible. If coadministered, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole level and antifungal response.
	NVP	↓ itraconazole possible ↑ NVP possible	Avoid combination if possible. If coadministered, monitor itraconazole concentration and adjust dose accordingly.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection. (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with itraconazole.)
Posaconazole	EFV	posaconazole AUC ↓ 50% ↔ EFV	Avoid concomitant use unless the benefit outweighs the risk. If coadministered, monitor posaconazole concentration and adjust dose accordingly.
	ETR	↑ ETR possible	No dosage adjustment necessary.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection. (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with posaconazole.)
Voriconazole	EFV	voriconazole AUC ↓ 77% EFV AUC ↑ 44%	**Contraindicated at standard doses.** Dose: voriconazole 400 mg BID, EFV 300 mg daily.
	ETR	voriconazole AUC ↑ 14% ETR AUC ↑ 36%	No dosage adjustment necessary; use with caution. Consider monitoring voriconazole level.
	NVP	↓ voriconazole possible ↑ NVP possible	Monitor for toxicity and antifungal response and/or voriconazole level.
	RPV	↑ RPV possible	No dosage adjustment necessary. Clinically monitor for breakthrough fungal infection. (RPV 150 mg/day reduces ketoconazole exposure; no data on interaction with voriconazole.)
Antimycobacterials			
Clarithromycin	EFV	clarithromycin AUC ↓ 39%	Monitor for effectiveness or consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Page 3 of 6)*

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimycobacterials, cont'd			
Clarithromycin, cont'd	ETR	clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	NVP	clarithromycin AUC ↓ 31%	Monitor for effectiveness or use alternative agent, such as azithromycin, for MAC prophylaxis and treatment.
	RPV	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide, such as azithromycin, for MAC prophylaxis and treatment.
Rifabutin	EFV	rifabutin ↓ 38%	Dose: rifabutin 450–600 mg once daily or 600 mg three times a week if EFV is not coadministered with a PI.
	ETR	rifabutin and metabolite AUC ↓ 17% ETR AUC ↓ 37%	**If ETR is used with an RTV-boosted PI, rifabutin should not be coadministered.** Dose: rifabutin 300 mg once daily if ETR is not coadministered with an RTV-boosted PI.
	NVP	rifabutin AUC ↑ 17% and metabolite AUC ↑ 24% NVP C_{min} ↓ 16%	No dosage adjustment necessary. Use with caution.
	RPV	RPV AUC ↓ 46%	**Contraindicated. Do not coadminister.**
Rifampin	EFV	EFV AUC ↓ 26%	Maintain EFV dose at 600 mg once daily and monitor for virologic response. Consider therapeutic drug monitoring. Some clinicians suggest EFV 800 mg dose in patients who weigh more than 60 kg.
	ETR	Significant ↓ ETR possible	**Do not coadminister.**
	NVP	NVP ↓ 20%–58%	**Do not coadminister.**
	RPV	RPV AUC ↓ 80%	**Contraindicated. Do not coadminister.**
Rifapentine	EFV, ETR, NVP, RPV	↓ NNRTI expected	**Do not coadminister.**
Benzodiazepines			
Alprazolam	EFV, ETR, NVP, RPV	No data	Monitor for therapeutic effectiveness of alprazolam.
Diazepam	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary.
Lorazepam	EFV	lorazepam C_{max} ↑ 16%, AUC ↔	No dosage adjustment necessary.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Page 4 of 6)*

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Midazolam	EFV	Significant ↑ midazolam expected	**Do not coadminister with oral midazolam.** Parenteral midazolam can be used with caution as a single dose and can be given in a monitored situation for procedural sedation.
Triazolam	EFV	Significant ↑ triazolam expected	**Do not coadminister.**
Cardiac Medications			
Dihydropyridine calcium channel blockers (CCBs)	EFV, NVP	↓ CCBs possible	Titrate CCB dose based on clinical response.
Diltiazem **Verapamil**	EFV	diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	NVP	↓ diltiazem or verapamil possible	
Corticosteroids			
Dexamethasone	EFV, ETR, NVP	↓ EFV, ETR, NVP possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV	Significant ↓ RPV possible	**Contraindicated with more than a single dose of dexamethasone.**
Hepatitis C NS3/4A - Protease Inhibitors			
Boceprevir	EFV	EFV AUC ↑ 20% boceprevir AUC ↓ 19%, C_{min} ↓ 44%	**Coadministration is not recommended.**
Telaprevir	EFV	EFV AUC ↔ telaprevir AUC ↓ 26%, C_{min} ↓ 47% With TDF: EFV AUC ↓ 15%–18%, telaprevir AUC ↓ 18%–20%	Increase telaprevir dose to 1125 mg q8h.
Herbal Products			
St. John's wort	EFV, ETR, NVP, RPV	↓ NNRTI	**Do not coadminister.**

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Page 5 of 6)*

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Contraceptives			
Hormonal contraceptives	EFV	ethinyl estradiol ↔ levonorgestrel AUC ↓ 83% norelgestromin AUC ↓ 64% ↓ etonogestrel (implant) possible	Use alternative or additional contraceptive methods. Norelgestromin and levonorgestrel are active metabolites of norgestimate.
	ETR	ethinyl estradiol AUC ↑ 22% norethindrone: no significant effect	No dosage adjustment necessary.
	NVP	ethinyl estradiol AUC ↓ 20% norethindrone AUC ↓ 19%	Use alternative or additional contraceptive methods.
		DMPA: no significant change	No dosage adjustment necessary.
	RPV	ethinyl estradiol AUC ↑ 14% norethindrone: no significant change	No dosage adjustment necessary.
Levonorgestrel (for emergency contraception)	EFV	levonorgestrel AUC ↓ 58%	Effectiveness of emergency postcoital contraception may be diminished.
HMG-CoA Reductase Inhibitors			
Atorvastatin	EFV, ETR	atorvastatin AUC ↓ 32%–43%	Adjust atorvastatin according to lipid responses, not to exceed the maximum recommended dose.
	RPV	Atorvastatin AUC ↔ Atorvastatin metabolites ↑	No dosage adjustment necessary.
Fluvastatin	ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary.
Lovastatin **Simvastatin**	EFV	simvastatin AUC ↓ 68%	Adjust simvastatin dose according to lipid responses, not to exceed the maximum recommended dose. If EFV used with RTV-boosted PI, simvastatin and lovastatin should be avoided.
	ETR, NVP	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid responses, not to exceed the maximum recommended dose. If ETR or NVP used with RTV-boosted PI, simvastatin and lovastatin should be avoided.
Pitavastatin	EFV, ETR, NVP, RPV	No data	No dosage recommendation.
Pravastatin **Rosuvastatin**	EFV	pravastatin AUC ↓ 44% rosuvatatin: no data	Adjust statin dose according to lipid responses, not to exceed the maximum recommended dose.
	ETR	No significant effect expected	No dosage adjustment necessary.

Table 15b. Drug Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Page 6 of 6)*

Concomitant Drug Class/Name	NNRTI[a]	Effect on NNRTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	EFV	buprenorphine AUC ↓ 50% norbuprenorphine[b] AUC ↓ 71%	No withdrawal symptoms reported. No dosage adjustment recommended, but monitor for withdrawal symptoms.
	ETR	buprenorphine AUC ↓ 25%	No dosage adjustment necessary.
	NVP	No significant effect	No dosage adjustment necessary.
Methadone	EFV	methadone AUC ↓ 52%	Opioid withdrawal common; increased methadone dose often necessary.
	ETR	No significant effect	No dosage adjustment necessary.
	NVP	methadone AUC ↓ 37%–51% NVP: no significant effect	Opioid withdrawal common; increased methadone dose often necessary.
	RPV	R-methadone[c] AUC ↓ 16%	No dosage adjustment necessary, but monitor for withdrawal symptoms.
Phosphodiesterase Type 5 (PDE5) Inhibitors			
Sildenafil	ETR	sildenafil AUC ↓ 57%	May need to increase sildenafil dose based on clinical effect.
	RPV	sildenafil ↔	No dosage adjustment necessary.
Tadalafil	ETR	↓ tadalafil possible	May need to increase tadalafil dose based on clinical effect.
Vardenafil	ETR	↓ vardenafil possible	May need to increase vardenafil dose based on clinical effect.
Miscellaneous Interactions			
Atovaquone/proguanil	EFV	↓ atovaquone AUC 75% ↓ progaunil AUC 43%	No dosage recommendation. Consider alternative drug for malaria prophylaxis, if possible.

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 to 150 mg per dose.

[b] Norbuprenorphine is an active metabolite of buprenorphine.

[c] R-methadone is the active form of methadone.

Key to Abbreviations: ARV = antiretroviral, AUC = area under the curve, BID = twice daily, CCB = calcium channel blocker, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, DLV = delavirdine, DMPA = depomedroxyprogesterone acetate, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, INR = international normalized ratio, MAC = *Mycobacterium avium* complex, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PDE5 = phosphodiesterase type 5, PI = protease inhibitor, PPI = proton pump inhibitor, RPV = rilpivirine, RTV = ritonavir, TDF = tenofivir

Table 15c. Drug Interactions between Nucleoside Reverse Transriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Page 1 of 2)

Concomitant Drug Class/ Name	NRTI	Effect on NRTI or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
Antivirals			
Boceprevir	TDF	No significant PK effects	No dose adjustment necessary.
Ganciclovir Valganciclovir	TDF	No data	Serum concentrations of these drugs and/or TDF may be increased. Monitor for dose-related toxicities.
	ZDV	No significant PK effects	Potential increase in hematologic toxicities
Ribavirin	ddI	↑ intracellular ddI	**Contraindicated. Do not coadminister.** Fatal hepatic failure and other ddI-related toxicities have been reported with coadministration.
	ZDV	Ribavirin inhibits phosphorylation of ZDV.	Avoid coadministration if possible or closely monitor virologic response and hematologic toxicities.
Telaprevir	TDF	TDF AUC ↑ 30%, C_{min} ↑ 6%–41%	Monitor for TDF-associated toxicity.
Integrase Inhibitor			
RAL	TDF	RAL AUC ↑ 49%, C_{max} ↑ 64%	No dosage adjustment necessary.
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	3TC, ddI, TDF, ZDV	No significant effect	No dosage adjustment necessary.
Methadone	ABC	methadone clearance ↑ 22%	No dosage adjustment necessary.
	d4T	d4T AUC ↓ 23%, C_{max} ↓ 44%	No dosage adjustment necessary.
	ZDV	ZDV AUC ↑ 29%–43%	Monitor for ZDV-related adverse effects.
NRTIs			
ddI	d4T	No significant PK interaction	**Avoid coadministration.** Additive toxicities of peripheral neuropathy, lactic acidosis, and pancreatitis seen with this combination.
	TDF	ddI-EC AUC and C_{max} ↑ 48%–60%	**Avoid coadministration.**
Other			
Allopurinol	ddI	ddI AUC ↑ 113% In patients with renal impairment: ddI AUC ↑ 312%	**Contraindicated. Do not coadminister.** Potential for increased ddI-associated toxicities.
PIs			
ATV	ddI	With ddI-EC + ATV (with food): ddI AUC ↓ 34%; ATV no change	Administer ATV with food 2 hours before or 1 hour after didanosine.
	TDF	ATV AUC ↓ 25% and C_{min} ↓ 23%–40% (higher C_{min} with RTV than without RTV) TDF AUC ↑ 24%–37%	Dose: ATV/r 300/100 mg daily coadministered with TDF 300 mg daily. Avoid concomitant use without RTV. If using TDF and H2 receptor antagonist in ART-experienced patients, use ATV/r 400 mg/100 mg daily. Monitor for TDF-associated toxicity.
	ZDV	ZDV C_{min} ↓ 30%, no change in AUC	Clinical significance unknown.

Table 15c. Drug Interactions between Nucleoside Reverse Transriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Page 2 of 2)

Concomitant Drug Class/ Name	NRTI	Effect on NRTI or Concomitant Drug Concentrations	Dosage Recommendations and Clinical Comments
DRV/r	TDF	TDF AUC ↑ 22%, C_{max} ↑ 24%, and C_{min} ↑ 37%	Clinical significance unknown. Monitor for TDF toxicity.
LPV/r	TDF	LPV/r AUC ↓ 15% TDF AUC ↑ 34%	Clinical significance unknown. Monitor for TDF toxicity.
TPV/r	ABC	ABC AUC ↓ 35%–44%	Appropriate doses for this combination have not been established.
	ddI	ddI-EC AUC ↔ and C_{min} ↓ 34% TPV/r ↔	Separate doses by at least 2 hours.
	TDF	TDF AUC ↔ TPV/r AUC ↓ 9%–18% and C_{min} ↓ 12%–21%	No dosage adjustment necessary.
	ZDV	ZDV AUC ↓ 35% TPV/r AUC ↓ 31%–43%	Appropriate doses for this combination have not been established.

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ART = antiretroviral, ATV = atazanavir, ATV/r = atazanavir/ritonavir, AUC = area under the curve, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, d4T = stavudine, ddI = didanosine, DRV/r = darunavir/ritonavir, EC = enteric coated, LPV/r = lopinavir/ritonavir, NRTI = nucleoside reverse transcriptase inhibitor, PI = protease inhibitor, PK = pharmacokinetic, RAL = raltegravir, TDF = tenofovir, TPV/r = tipranavir/ritonavir, ZDV = zidovudine

Table 15d. Drug Interactions between CCR5 Antagonist and Other Drugs

This table provides information relating to PK interactions between MVC and non-ARV drugs. For interactions among ARV agents and for dosing recommendations, please refer to Table 16b.

Concomitant Drug Class/Name	CCR5 Antagonist	Effect on CCR5 Antagonist or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticonvulsants			
Carbamazepine Phenobarbital Phenytoin	MVC	↓ MVC possible	If used without a strong CYP3A inhibitor, use MVC 600 mg BID or an alternative antiepileptic agent.
Antifungals			
Itraconazole	MVC	↑ MVC possible	Dose: MVC 150 mg BID
Ketoconazole	MVC	MVC AUC ↑ 400%	Dose: MVC 150 mg BID
Voriconazole	MVC	↑ MVC possible	Consider dose reduction to MVC 150 mg BID
Antimycobacterials			
Clarithromycin	MVC	↑ MVC possible	Dose: MVC 150 mg BID
Rifabutin	MVC	↓ MVC possible	If used without a strong CYP3A inducer or inhibitor, use MVC 300 mg BID. If used with a strong CYP3A inhibitor, use MVC 150 mg BID.
Rifampin	MVC	MVC AUC ↓ 64%	Coadministration is not recommended. If coadministration is necessary, use MVC 600 mg BID. If coadministered with a strong CYP3A inhibitor, use MVC 300 mg BID.
Rifapentine	MVC	↓ MVC expected	**Do not coadminister.**
Herbal Products			
St. John's wort	MVC	↓ MVC possible	**Coadministration is not recommended.**
Hormonal Contraceptives			
Hormonal contraceptives	MVC	No significant effect on ethinyl estradiol or levonorgestrel	Safe to use in combination
Narcotics/Treatment for Opioid Dependence			
Methadone	MVC	No data	

Key to Abbreviations: ARV = antiretroviral, AUC = area under the curve, BID = twice daily, CYP = cytochrome P, MVC = maraviroc, PK = pharmacokinetic

Table 15e. Drug Interactions between Integrase Inhibitor and Other Drugs

Concomitant Drug Class/Name	Integrase Inhibitor	Effect on Integrase Inhibitor or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Omeprazole	RAL	RAL AUC ↑ 212%, C_{max} ↑ 315%, and C_{min} ↑ 46%	No dosage adjustment necessary.
Antimycobacterials			
Rifabutin	RAL	RAL AUC ↑ 19%, C_{max} ↑ 39%, and C_{min} ↓ 20%	No dosage adjustment necessary.
Rifampin	RAL	RAL 400 mg: RAL AUC ↓ 40% and C_{min} ↓ 61% Rifampin with RAL 800 mg BID compared with RAL 400 mg BID alone: RAL AUC ↑ 27% and C_{min} ↓ 53%	Dose: RAL 800 mg BID Monitor closely for virologic response.
Hepatitis C NS3/4A – Protease Inhibitors			
Boceprevir	RAL	No significant effect	No dosage adjustment necessary.
Telaprevir	RAL	RAL AUC ↑ 31% Telaprevir ↔	No dosage adjustment necessary.
Hormonal Contraceptives			
Hormonal contraceptives	RAL	No clinically significant effect	Safe to use in combination
Narcotics/Treatment for Opioid Dependence			
Buprenorphine	RAL	No significant effect	No dosage adjustment necessary.
Methadone	RAL	No significant effect	No dosage adjustment necessary.

Key to Abbreviations: AUC = area under the curve, BID = twice daily, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, RAL = raltegravir

*Table 16a. Interactions Among Protease Inhibitors**

*NFV and IDV are not included in this table. Please refer to NFV and IDV FDA package inserts for information regarding NFV and IDV drug interactions.

Drug Affected	ATV	FPV	LPV/r	RTV	SQV	TPV
DRV	Dose: ATV 300 mg once daily + DRV 600 mg BID + RTV 100 mg BID	No data	**Should not be coadministered because doses are not established**	Dose: (DRV 600 mg + RTV 100 mg) BID or (DRV 800 mg + RTV 100 mg) once daily	**Should not be coadministered because doses are not established**	No data
FPV	Dose: Insufficient data	•	**Should not be coadministered because doses are not established**	Dose: (FPV 1400 mg + RTV 100 mg or 200 mg) once daily; or (FPV 700 mg + RTV 100 mg) BID	Dose: Insufficient data	**Should not be coadministered because doses are not established**
LPV/r	Dose: ATV 300 mg once daily + LPV/r 400/100 mg BID	**Should not be coadministered because doses are not established**	•	LPV is coformulated with RTV as Kaletra.	Dose: SQV 1000 mg BID + LPV/r 400/100 mg BID	**Should not be coadministered because doses are not established**
RTV	Dose: (ATV 300 mg + RTV 100 mg) once daily	Dose: (FPV 1400 mg + RTV 100 mg or 200 mg) once daily; or (FPV 700 mg + RTV 100 mg) BID	LPV is coformulated with RTV and marketed as Kaletra.	•	Dose: (SQV 1000 mg + RTV 100 mg) BID	Dose: (TPV 500 mg + RTV 200 mg) BID
SQV	Dose: Insufficient data	Dose: Insufficient data	Dose: SQV 1000 mg BID + LPV/r 400/100 mg BID	Dose: (SQV 1000 mg + RTV 100 mg) BID	•	**Should not be coadministered because doses are not established**

Key to Abbreviations: ATV = atazanavir, BID = twice daily, DRV = darunavir, FDA = Food and Drug Administration, FPV = fosamprenavir, IDV = indinavir, LPV/r = lopinavir/ritonavir, NFV = nelfinavir, PI = protease inhibitor, RTV = ritonavir, SQV = saquinavir, TPV = tipranavir

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, Maraviroc, Raltegravir, and Protease Inhibitors* (Page 1 of 3)*

*DLV, IDV, and NFV are not included in this table. Refer to the DLV, IDV, and NFV FDA package inserts for information regarding drug interactions.

		EFV	ETR	NVP	RPV[a]	MVC	RAL
ATV +/- RTV	**PK data**	With unboosted ATV ATV: AUC ↓ 74% EFV: no significant change With (ATV 300 mg + RTV 100 mg) once daily with food ATV concentrations similar to unboosted ATV without EFV	With unboosted ATV ETR: AUC ↑ 50%, C_{max} ↑ 47%, and C_{min} ↑ 58% ATV: AUC ↓ 17% and C_{min} ↓ 47% With (ATV 300 mg + RTV 100 mg) once daily ETR: AUC, C_{max}, and C_{min} ↑ approximately 30% ATV: AUC ↓ 14% and C_{min} ↓ 38%	With (ATV 300 mg + RTV 100 mg) once daily ATV: AUC ↓ 42% and C_{min} ↓ 72% NVP: AUC ↑ 25%	With boosted and unboosted ATV ↑ RPV possible	With unboosted ATV MVC: AUC ↑ 257% With (ATV 300 mg + RTV 100 mg) once daily MVC: AUC ↑ 388%	With unboosted ATV RAL: AUC ↑ 72% With (ATV 300 mg + RTV 100 mg) once daily RAL: AUC ↑ 41%
	Dose	**Do not coadminister with unboosted ATV.** In ART-naive patients (ATV 400 mg + RTV 100 mg) once daily **Do not coadminister in ART-experienced patients.**	**Do not coadminister with ATV +/– RTV.**	**Do not coadminister with ATV +/– RTV.**	Standard	MVC 150 mg BID with ATV +/– RTV	Standard
DRV – always use with RTV	**PK data**	With (DRV 300 mg + RTV 100 mg) BID DRV: AUC ↓ 13%, C_{min} ↓ 31% EFV: AUC ↑ 21%	ETR 100 mg BID with (DRV 600 mg + RTV 100 mg) BID DRV: no significant change ETR: AUC ↓ 37%, C_{min} ↓ 49%	With (DRV 400 mg + RTV 100 mg) BID DRV: AUC ↑ 24%[b] NVP: AUC ↑ 27% and C_{min} ↑ 47%	RPV 150 mg once daily with (DRV 800 mg + RTV 100 mg) once daily DRV: no significant change RPV: AUC ↑ 130% and C_{min} ↑ 178%	With (DRV 600 mg + RTV 100 mg) BID MVC: AUC ↑ 305% With (DRV 600 mg + RTV 100 mg) BID + ETR MVC: AUC ↑ 210%	With (DRV 600 mg + RTV 100 mg) BID RAL: AUC ↓ 29% and C_{min} ↑ 38%
	Dose	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	Standard (ETR 200 mg BID) Despite decreased ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	Standard	Standard	MVC 150 mg BID	Standard
EFV	**PK data**	•	↓ ETR possible	NVP: no significant change EFV: AUC ↓ 22%	↓ RPV possible	MVC: AUC ↓ 45%	EFV: AUC ↓ 36%
	Dose		**Do not coadminister.**	**Do not coadminister.**	**Do not coadminister.**	MVC: 600 mg BID	Standard

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, Maraviroc, Raltegravir, and Protease Inhibitors* (Page 2 of 3)*

		EFV	ETR	NVP	RPV[a]	MVC	RAL
ETR	**PK data**	↓ ETR possible	•	↓ ETR possible	↓ RPV possible	MVC: AUC ↓ 53%, C_{max} ↓ 60%	ETR: C_{min} ↓ 17% RAL: C_{min} ↓ 34%
	Dose	**Do not coadminister.**		**Do not coadminister.**	**Do not coadminister.**	MVC 600 mg BID in the absence of a potent CYP3A inhibitor	Standard
FPV	**PK data**	With (FPV 1400 mg + RTV 200 mg) once daily APV: C_{min} ↓ 36%	With (FPV 700 mg + RTV 100 mg) BID APV: AUC ↑ 69%, C_{min} ↑ 77%	With unboosted FPV 1400 mg BID APV: AUC ↓ 33% NVP: AUC ↑ 29% With (FPV 700 mg + RTV 100 mg) BID NVP: C_{min} ↑ 22%	With boosted and unboosted FPV ↑ RPV possible	Unknown; ↑ MVC possible	No data
	Dose	(FPV 1400 mg + RTV 300 mg) once daily or (FPV 700 mg + RTV 100 mg) BID EFV standard	**Do not coadminister with FPV +/– RTV.**	(FPV 700 mg + RTV 100 mg) BID NVP standard	Standard	MVC 150 mg BID	Standard
LPV/r	**PK data**	With LPV/r tablets 500/125 mg[c] BID + EFV 600 mg LPV levels similar to LPV/r 400/100 mg BID without EFV	With LPV/r tablets ETR: levels ↓ 30%–45% (comparable to the decrease with DRV/r) LPV: levels ↓ 13%–20%	With LPV/r capsules LPV: AUC ↓ 27% and C_{min} ↓51%	RPV 150 mg once daily with LPV/r capsules LPV: no significant change RPV: AUC ↑ 52% and C_{min} ↑ 74%	MVC: AUC ↑ 295% With LPV/r + EFV MVC: AUC ↑ 153%	↓ RAL ↔ LPV/r
	Dose	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID EFV standard	Standard	LPV/r tablets 500/125 mg[c] BID; LPV/r oral solution 533/133 mg BID NVP standard	Standard	MVC 150 mg BID	Standard
NVP	**PK data**	NVP: no significant change EFV: AUC ↓ 22%	↓ ETR possible	•	↓ RPV possible	MVC: AUC ↔ and C_{max} ↑ 54%	No data
	Dose	**Do not coadminister.**	**Do not coadminister.**		**Do not coadminister.**	Without PI MVC 300 mg BID With PI (except TPV/r) MVC 150 mg BID	Standard
RAL	**PK data**	RAL: AUC ↓ 36%	ETR: C_{min} ↑ 17% RAL: C_{min} ↓ 34%	No data	No data	RAL: AUC ↓ 37% MVC: AUC ↓ 21%	•
	Dose	Standard	Standard	No data	No data	Standard	

Table 16b. Interactions between Non-Nucleoside Reverse Transcriptase Inhibitors, Maraviroc, Raltegravir, and Protease Inhibitors* (Page 3 of 3)*

		EFV	ETR	NVP	RPV[a]	MVC	RAL
RPV	**PK data**	↓ RPV possible	↓ RPV possible	↓ RPV possible	•	No data	No data
	Dose	**Do not coadminister.**	**Do not coadminister.**	**Do not coadminister.**		No data	No data
RTV	**PK data**	Refer to information for boosted PI.	Refer to information for boosted PI.	Refer to information for boosted PI.	Refer to information for boosted PI.	With RTV 100 mg BID MVC: AUC ↑ 161%	With RTV 100 mg BID RAL: AUC ↓ 16%
	Dose					MVC 150 mg BID	Standard
SQV – always use with RTV	**PK data**	With SQV 1200 mg TID SQV: AUC ↓ 62% EFV: AUC ↓ 12%	With (SQV 1000 mg + RTV 100 mg) BID SQV: AUC unchanged ETR: AUC ↓ 33%, C_{min} ↓ 29% Reduced ETR levels similar to reduction with DRV/r	With 600 mg TID SQV: AUC ↓ 24% NVP: no significant change	↑ RPV possible	With (SQV 1000 mg + RTV 100 mg) BID MVC: AUC ↑ 877% With (SQV 1000 mg + RTV 100 mg) BID + EFV MVC: AUC ↑ 400%	No data
	Dose	(SQV 1000 mg + RTV 100 mg) BID	(SQV 1000 mg + RTV 100 mg) BID	Dose with SQV/r not established	Standard	MVC 150 mg BID	Standard
TPV – always use with RTV	**PK data**	With (TPV 500 mg + RTV 100 mg) BID TPV: AUC ↓ 31%, C_{min} ↓ 42% EFV: no significant change With (TPV 750 mg + RTV 200 mg) BID TPV: no significant change EFV: no significant change	With (TPV 500 mg + RTV 200 mg) BID ETR: AUC ↓ 76%, C_{min} ↓ 82% TPV: AUC ↑ 18%, C_{min} ↑ 24%	With (TPV 250 mg + RTV 200 mg) BID and with (TPV 750 mg + RTV 100 mg) BID NVP: no significant change TPV: no data	↑ RPV possible	With (TPV 500 mg + RTV 200 mg) BID MVC: no significant change in AUC TPV: no data	With (TPV 500 mg + RTV 200 mg) BID RAL: AUC ↓ 24%
	Dose	Standard	**Do not coadminister.**	Standard	Standard	MVC 300 mg BID	Standard

[a] Approved dose for RPV is 25 mg once daily. Most PK interaction studies were performed using 75 to 150 mg per dose.

[b] Based on between-study comparison.

[c] Use a combination of two LPV/r 200 mg/50 mg tablets + one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg.

Key to Abbreviations: APV = amprenavir, ART = antiretroviral therapy, ATV = atazanavir, AUC = area under the curve, BID = twice daily, C_{max} = maximum plasma concentration, C_{min} = minimum plasma concentration, CYP = cytochrome P, DLV = delavirdine, DRV = darunavir, DRV/r = darunavir/ritonavir, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, FPV = fosamprenavir, IDV = indinavir, LPV = lopinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NVP = nevirapine, PI = protease inhibitor, PK = pharmacokinetic, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, SQV/r = saquinarir/ritonavir, TID = three times a day, TPV = tipranavir

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Last updated March 27, 2012; last reviewed March 27, 2012) (page 1 of 3)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Intracellular Half-lives	Adverse Events (Also see Table 13)
Abacavir (ABC)/Ziagen **Also available as component of fixed-dose combinations:**	Ziagen • 300-mg tablets • 120-mg/mL oral solution	Ziagen 300 mg BID or 600 mg once daily Take without regard to meals	Metabolized by alcohol dehydrogenase and glucuronyl transferase Renal excretion of metabolites 82% Dosage adjustment for ABC recommended in patients with hepatic insufficiency (See Appendix B, Table 7.)	1.5 hrs/ 12–26 hrs	• HSRs: Patients who test positive for HLA-B*5701 are at highest risk. HLA screening should be done before initiation of ABC. Rechallenge is not recommended. • Symptoms of HSR may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, or fatigue or respiratory symptoms such as sore throat, cough, or shortness of breath. • Some cohort studies suggest increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.
Trizivir ABC with ZDV+3TC	Trizivir (ABC 300 mg + ZDV 300 mg + 3TC 150 mg) tablet	Trizivir 1 tablet BID			
Epzicom ABC with 3TC	Epzicom (ABC 600 mg + 3TC 300 mg) tablet	Epzicom 1 tablet once daily			
Didanosine (ddI)/ Videx EC (generic available; dose same as Videx EC)	Videx EC 125-, 200-, 250-, 400-mg capsules Videx 10-mg/mL oral solution	**Body weight ≥60kg:** 400 mg once daily *With TDF:* 250 mg once daily **Body weight <60kg:** 250 mg once daily *With TDF:* 200 mg once daily Take 1/2 hour before or 2 hours after a meal Note: Preferred dosing with oral solution is BID (total daily dose divided into 2 doses)	Renal excretion 50% Dosage adjustment in patients with renal insufficiency recommended (See Appendix B, Table 7.)	1.5 hrs/ >20 hrs	• Pancreatitis • Peripheral neuropathy • Retinal changes, optic neuritis • Lactic acidosis with hepatic steatosis +/- pancreatitis (rare but potentially life-threatening toxicity) • Nausea, vomiting • Potential association with noncirrhotic portal hypertension, in some cases, patients presented with esophageal varices • One cohort study suggested increased risk of MI with recent or current use of ddI, but this risk is not substantiated in other studies. • Insulin resistance/diabetes mellitus

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Last updated March 27, 2012; last reviewed March 27, 2012) (page 2 of 3)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Intracellular Half-lives	Adverse Events (Also see Table 13)
Emtricitabine (FTC)/Emtriva **Also available as component of fixed-dose combinations:**	Emtriva • 200-mg hard gelatin capsule • 10-mg/mL oral solution	Emtriva *Capsule:* 200 mg once daily *Oral solution:* 240 mg (24 mL) once daily Take without regard to meals	Renal excretion 86% Dosage adjustment in patients with renal insufficiency recommended (See Appendix B, Table 7.)	10 hrs/ >20 hrs	• Minimal toxicity • Hyperpigmentation/skin discoloration • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue FTC.
Atripla FTC with EFV+TDF	Atripla (FTC 200 mg + EFV 600 mg + TDF 300 mg) tablet	Atripla 1 tablet at or before bedtime Take on an empty stomach to reduce side effects			
Complera FTC with RPV+TDF	Complera (FTC 200 mg + RPV 25 mg + TDF 300 mg) tablet	Complera 1 tablet once daily with a meal			
Truvada FTC with TDF	Truvada FTC 200 mg + TDF 300 mg tablet	Truvada 1 tablet once daily			
Lamivudine (3TC)/ Epivir (generic available) **Also available as component of fixed-dose combinations:**	Epivir • 150-, 300-mg tablets • 10-mg/mL oral solution	Epivir 150 mg BID or 300 mg once daily Take without regard to meals	Renal excretion 70% Dosage adjustment in patients with renal insufficiency recommended (See Appendix B, Table 7.)	5–7 hrs/ 18–22 hrs	• Minimal toxicity • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue 3TC.
Combivir (generic available) 3TC with ZDV	Combivir (3TC 150 mg + ZDV 300 mg) tablet	Combivir 1 tablet BID			
Epzicom 3TC with ABC	Epzicom (3TC 300 mg + ABC 600 mg) tablet	Epzicom 1 tablet once daily			
Trizivir 3TC with ZDV+ABC	Trizivir (3TC 150 mg + ZDV 300 mg + ABC 300 mg) tablet	Trizivir 1 tablet BID			
Stavudine (d4T)/ Zerit (generic available)	Zerit • 15-, 20-, 30-, 40-mg capsules • 1-mg/mL oral solution	**Body weight ≥60 kg:** 40 mg BID **Body weight <60 kg:** 30 mg BID Take without regard to meals Note: WHO recommends 30 mg BID dosing regardless of body weight.	Renal excretion 50% Dosage adjustment in patients with renal insufficiency recommended (See Appendix B, Table 7.)	1 hr/ 7.5 hrs	• Peripheral neuropathy • Lipoatrophy • Pancreatitis • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes mellitus • Rapidly progressive ascending neuromuscular weakness (rare)

Appendix B, Table 1. Characteristics of Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Last updated March 27, 2012; last reviewed March 27, 2012) (page 3 of 3)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Intracellular Half-lives	Adverse Events (Also see Table 13)
Tenofovir Disoproxil Fumarate (TDF)/Viread **Also available as component of fixed-dose combinations:**	Viread • 150-, 200-, 250-, 300-mg tablets • 40-mg/g oral powder	Viread 300 mg once daily 7.5 scoops once daily Take without regard to meals Mix oral powder with 2–4 ounces of food not requiring chewing (e.g., applesauce, yogurt). **Do not mix oral powder with liquid.**	Renal excretion 86% Dosage adjustment in patients with renal insufficiency recommended (See Appendix B, Table 7.)	17 hrs/ >60 hrs	• Renal insufficiency, Fanconi syndrome • Osteomalacia, decrease in bone mineral density • Potential decrease in bone mineral density • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDF. • Asthenia, headache, diarrhea, nausea, vomiting, and flatulence
Atripla TDF with EFV+FTC	Atripla (TDF 300 mg + EFV 600 mg + FTC 200 mg) tablet	Atripla 1 tablet at or before bedtime Take on an empty stomach to reduce side effects			
Complera TDF with RPV+FTC	Complera (TDF 300 mg + RPV 25 mg + FTC 200 mg) tablet	Complera 1 tablet once daily Take with a meal			
Truvada TDF with FTC	Truvada (TDF 300 mg + FTC 200 mg) tablet	Truvada 1 tablet once daily Take without regard to meals			
Zidovudine (ZDV)/ Retrovir (generic available) **Also available as component of fixed-dose combinations:**	Retrovir • 100-mg capsule • 300-mg tablet • 10-mg/mL intravenous solution • 10-mg/mL oral solution	Retrovir 300 mg BID or 200 mg TID Take without regard to meals	Metabolized to GAZT Renal excretion of GAZT Dosage adjustment in patients with renal insufficiency recommended (See Appendix B, Table 7.)	1.1 hrs/ 7 hrs	• Bone marrow suppression: macrocytic anemia or neutropenia • Nausea, vomiting, headache, insomnia, asthenia • Nail pigmentation • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes mellitus • Lipoatrophy • Myopathy
Combivir (generic available) ZDV with 3TC	Combivir (ZDV 300 mg + 3TC 150 mg) tablet	Combivir 1 tablet BID			
Trizivir ZDV with 3TC+ABC	Trizivir (ZDV 300 mg + 3TC 150 mg + ABC 300 mg) tablet	Trizivir 1 tablet BID			

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, BID = twice daily, d4T = stavudine, ddI = didanosine, EC = enteric coated, EFV = efavirenz, FTC = emtricitabine, GAZT = azidothymidine glucuronide, HBV = hepatitis B virus, HLA = human leukocyte antigen, HSR = hypersensitivity reaction, MI = myocardial infarction, RPV = rilpivirine, TDF = tenofovir disoproxil fumarate, TID = three times a day, WHO = World Health Organization, ZDV = zidovudine

Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors* (NNRTIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 1 of 2)

*DLV is not included in this table. Please refer to the DLV FDA package insert for related information.

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Adverse Events (Also see Table 13)
Efavirenz (EFV)/ Sustiva **Also available as component of fixed-dose combination:**	• 50-, 200-mg capsules • 600-mg tablet	600 mg once daily at or before bedtime Take on an empty stomach to reduce side effects.	Metabolized by CYPs 2B6 and 3A4 CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor)	40–55 hrs	• Rash[a] • Neuropsychiatric symptoms[b] • Increased transaminase levels • Hyperlipidemia • False-positive results with some cannabinoid and benzodiazepine screening assays reported. • Teratogenic in nonhuman primates and potentially teratogenic in humans
Atripla EFV with TDF + FTC	(EFV 600 mg + FTC 200 mg + TDF 300 mg) tablet	1 tablet once daily at or before bedtime.			
Etravirine (ETR)/ Intelence	• 100-, 200-mg tablets	200 mg BID Take following a meal.	CYP3A4, 2C9, and 2C19 substrate 3A4 inducer; 2C9 and 2C19 inhibitor	41 hrs	• Rash, including Stevens-Johnson syndrome[a] • HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure, have been reported. • Nausea
Nevirapine (NVP)/ Viramune or Viramine XR	• 200-mg tablet • 400-mg XR tablet • 50-mg/5-mL oral suspension	200 mg once daily for 14 days (lead-in period); thereafter, 200 mg BID or 400 mg (Viramune XR tablet) once daily Take without regard to meals. Repeat lead-in period if therapy is discontinued for more than 7 days. In patients who develop mild-to-moderate rash without constitutional symptoms, continue lead-in period until rash resolves but not longer than 28 days total.	CYP450 substrate, inducer of 3A4 and 2B6; 80% excreted in urine (glucuronidated metabolites, <5% unchanged); 10% in feces	25–30 hrs	• Rash, including Stevens-Johnson syndrome[a] • Symptomatic hepatitis, including fatal hepatic necrosis, has been reported: - rash reported in approximately 50% of cases; - occurs at significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts >250 cells/mm^3 and in ARV-naive male patients with pre-NVP CD4 counts >400 cells/mm^3. NVP should not be initiated in these patients unless the benefit clearly outweighs the risk.

Appendix B, Table 2. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors* (NNRTIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 2 of 2)

*DLV is not included in this table. Please refer to the DLV FDA package insert for related information.

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Adverse Events (Also see Table 13)
Rilpivirine (RPV)/ Edurant **Also available as component of fixed-dose combination:**	• 25-mg tablet	25 mg once daily Take with a meal.	CYP3A4 substrate	50 hrs	• Rash[a] • Depression, insomnia, headache
Complera RPV with TDF + FTC	Complera (RPV 25 mg + TDF 300 mg + FTC 200 mg) tablet	1 tablet once daily with a meal			

Key to Abbreviations: ARV = antiretroviral, BID = twice daily, CYP = cytochrome P, DLV = delavirdine, EFV = efavirenz, ETR = etravirine, FDA = Food and Drug Administration, FTC = emtricitabine, HSR = hypersensitivity reaction, NNRTI = non-nucleoside reverse transcriptase inhibitor, NVP = nevirapine, RPV = rilpivirine, TDF = tenofovir disoproxil fumarate, XR = extended release

[a] Rare cases of Stevens-Johnson syndrome have been reported with most NNRTIs; the highest incidence of rash was seen with NVP.

[b] Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of patients receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2 to 4 weeks but may necessitate discontinuation of EFV in a small percentage of patients.

Appendix B, Table 3. Characteristics of Protease Inhibitors (PIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 1 of 5)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Storage	Adverse Events (Also see Table 13)
Atazanavir (ATV)/ Reyataz	100-, 150-, 200-, 300-mg capsules	ARV-naive patients: 400 mg once daily or (ATV 300 mg + RTV 100 mg) once daily With TDF or in ARV-experienced patients: (ATV 300 mg + RTV 100 mg) once daily With EFV in ARV-naive patients: (ATV 400 mg + RTV 100 mg) once daily (For recommendations on dosing with H2 antagonists and PPIs, refer to Table 16a.) Take with food	CYP3A4 inhibitor and substrate Dosage adjustment in patients with hepatic insufficiency recommended (See Appendix B, Table 7.)	7 hrs	Room temperature (up to 25ºC or 77ºF)	• Indirect hyperbilirubinemia • PR interval prolongation: First degree symptomatic AV block reported. Use with caution in patients with underlying conduction defects or on concomitant medications that can cause PR prolongation. • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Nephrolithiasis • Skin rash (20%) • Serum transaminase elevations • Hyperlipidemia (especially with RTV boosting)
Darunavir (DRV)/ Prezista	75-, 150-, 300-, 400-, 600-mg tablets	ARV-naive patients or ARV-experienced patients with no DRV mutations: (DRV 800 mg + RTV 100 mg) once daily ARV-experienced patients with at least one DRV mutation: (DRV 600 mg + RTV 100 mg) BID **Unboosted DRV is not recommended** Take with food	CYP3A4 inhibitor and substrate	15 hrs (when combined with RTV)	Room temperature (up to 25ºC or 77ºF)	• Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome and erythrema multiforme have been reported. • Hepatotoxicity • Diarrhea, nausea • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

Appendix B, Table 3. Characteristics of Protease Inhibitors (PIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 2 of 5)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Storage	Adverse Events (Also see Table 13)
Fosamprenavir (FPV)/ Lexiva (a prodrug of amprenavir [APV])	• 700-mg tablet • 50-mg/mL oral suspension	ARV-naive patients: • FPV 1400 mg BID or • (FPV 1400 mg + RTV 100–200 mg) once daily or • (FPV 700 mg + RTV 100 mg) BID PI-experienced patients (once-daily dosing not recommended): • (FPV 700 mg + RTV 100 mg) BID With EFV: • (FPV 700 mg + RTV 100 mg) BID or • (FPV 1400 mg + RTV 300 mg) once daily *Tablet*: Take without regard to meals (if not boosted with RTV tablet) *Suspension*: Take without food *FPV with RTV tablet*: Take with meals	APV is a CYP3A4 substrate, inhibitor, and inducer Dosage adjustment in patients with hepatic insufficiency recommended (See Appendix B, Table 7.)	7.7 hrs (APV)	Room temperature (up to 25ºC or 77ºF)	• Skin rash (12%–19%): FPV has a sulfonamide moiety • Diarrhea, nausea, vomiting • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Nephrolithiasis
Indinavir (IDV)/ Crixivan	100-, 200-, 400-mg capsules	800 mg every 8 hrs Take 1 hour before or 2 hours after meals; may take with skim milk or low-fat meal With RTV: (IDV 800 mg + RTV 100–200 mg) BID Take without regard to meals	CYP3A4 inhibitor and substrate Dosage adjustment in patients with hepatic insufficiency recommended (See Appendix B, Table 7.)	1.5–2 hrs	Room temperature (15º–30ºC/ 59º–86ºF) Protect from moisture	• Nephrolithiasis • GI intolerance, nausea • Hepatitis • Indirect hyperbilirubinemia • Hyperlipidemia • Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

Appendix B, Table 3. Characteristics of Protease Inhibitors (PIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 3 of 5)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Storage	Adverse Events (Also see Table 13)
Lopinavir + Ritonavir (LPV/r)/ Kaletra	Tablets: (LPV 200 mg + RTV 50 mg) or (LPV 100 mg + RTV 25 mg) Oral solution: Each 5 mL contains (LPV 400 mg + RTV 100 mg) Oral solution contains 42% alcohol	LPV/r 400 mg/100 mg BID or LPV/r 800 mg/200 mg once daily Once-daily dosing is not recommended for patients with ≥3 LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital. With EFV or NVP (PI-naive or PI-experienced patients): LPV/r 500-mg/125-mg tablets BID (Use a combination of two LPV/r 200-mg/50-mg tablets + one LPV/r 100-mg/25-mg tablet to make a total dose of LPV/r 500 mg/125 mg.) or LPV/r 533-mg/133-mg oral solution BID *Tablet:* Take without regard to meals *Oral solution:* Take with food	CYP3A4 inhibitor and substrate	5–6 hrs	Oral tablet is stable at room temperature. Oral solution is stable at 2°–8°C (36°–46°F) until date on label and is stable for up to 2 months when stored at room temperature (up to 25ºC or 77ºF).	• GI intolerance, nausea, vomiting, diarrhea • Pancreatitis • Asthenia • Hyperlipidemia (especially hypertriglyceridemia) • Serum transaminase elevation • Hyperglycemia • Insulin resistance/diabetes mellitus • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval prolongation • QT interval prolongation and torsades de pointes have been reported; however, causality could not be established.
Nelfinavir (NFV)/ Viracept	• 250-, 625-mg tablets • 50-mg/g oral powder	1250 mg BID or 750 mg TID Dissolve tablets in a small amount of water, mix admixture well, and consume immediately. Take with food	CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP 3A4 inhibitor	3.5–5 hrs	Room temperature (15º–30ºC/ 59º–86ºF)	• Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Serum transaminase elevation

Appendix B, Table 3. Characteristics of Protease Inhibitors (PIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 4 of 5)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Storage	Adverse Events (Also see Table 13)
Ritonavir (RTV)/ Norvir	• 100-mg soft gel capsule • 100-mg tablet • 80-mg/mL oral solution Oral solution contains 43% alcohol.	As pharmacokinetic booster for other PIs: 100–400 mg per day in 1–2 divided doses (refer to other PIs for specific dosing recommendations) *Tablet:* Take with food *Capsule and oral solution:* To improve tolerability, take with food if possible.	CYP3A4 >2D6 substrate; potent 3A4, 2D6 inhibitor	3–5 hrs	Refrigerate capsules. Capsules can be left at room temperature (up to 25ºC or 77ºF) for up to 30 days. Tablets do not require refrigeration. Oral solution should not be refrigerated; store at room temperature 20º–25ºC (68º–77ºF).	• GI intolerance, nausea, vomiting, diarrhea • Paresthesias (circumoral and extremities) • Hyperlipidemia (especially hypertriglyceridemia) • Hepatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Saquinavir (SQV)/ Invirase	• 500-mg tablet • 200-mg hard gel capsule	(SQV 1000 mg + RTV 100 mg) BID Unboosted SQV is **not** recommended. Take with meals or within 2 hours after a meal.	CYP3A4 inhibitor and substrate	1–2 hrs	Room temperature (15º–30ºC/ 59º–86ºF)	• GI intolerance, nausea, and diarrhea • Headache • Serum transaminase elevation • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval prolongation • QT interval prolongation, torsades de pointes have been reported. Patients with pre-SQV QT interval >450 msec should not receive SQV (see Table 5b).

Appendix B, Table 3. Characteristics of Protease Inhibitors (PIs) (Last updated October 14, 2011; last reviewed March 27, 2012) (page 5 of 5)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in renal or hepatic insufficiency, see Appendix B, Table 7.)	Elimination	Serum/ Half-life	Storage	Adverse Events (Also see Table 13)
Tipranavir (TPV)/ Aptivus	• 250-mg capsule • 100-mg/mL oral solution	(TPV 500 mg + RTV 200 mg) BID Unboosted TPV is **not** recommended. *TPV taken with RTV **tablets**:* Take with meals. *TPV taken with RTV **capsules** or **solution**:* Take without regard to meals.	CYP P450 3A4 inducer and substrate Net effect when combined with RTV (CYP 3A4, 2D6 inhibitor)	6 hrs after single dose of TPV/r	Refrigerate capsules. Capsules can be stored at room temperature (25ºC or 77ºF) for up to 60 days. Oral solution should **not** be refrigerated or frozen and should be used within 60 days after bottle is opened.	• Hepatotoxicity: Clinical hepatitis (including hepatic decompensation and hepatitis-associated fatalities) has been reported; monitor closely, especially in patients with underlying liver diseases. • Skin rash (3%–21%): TPV has a sulfonamide moiety; use with caution in patients with known sulfonamide allergy. • Rare cases of fatal and nonfatal intracranial hemorrhages have been reported. Risks include brain lesion, head trauma, recent neurosurgery, coagulopathy, hypertension, alcoholism, use of anti-coagulant or anti-platelet agents including vitamin E. • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

Key to Abbreviations: APV = amprenavir, ARV = antiretroviral, ATV = atazanavir, AV = atrioventricular, BID = twice daily, CYP = cytochrome P, DRV = darunavir, EFV = efavirenz, FPV = fosamprenavir, GI = gastrointestinal, IDV = indinavir, LPV = lopinavir, LPV/r = lopinavir + ritonavir, msec = millisecond, NFV = nelfinavir, NVP = nevirapine, PI = protease inhibitor, PPI = proton pump inhibitor, RTV = ritonavir, SQV = saquinavir, TDF = tenofovir disoproxil fumarate, TID = three times a day, TPV = tipranavir

Appendix B, Table 4. Characteristics of Integrase Inhibitor (Last updated March 27, 2012; last reviewed March 27, 2012)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations (For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7.)	Serum/ Half-life	Route of Metabolism	Adverse Events (Also see Table 13)
Raltegravir (RAL)/ Isentress	• 400-mg tablet • 25-, 100-mg chewable tablets	400 mg BID **With rifampin:** 800 mg BID Take without regard to meals.	~9 hrs	UGT1A1-mediated glucuronidation	• Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis • Nausea • Headache • Diarrhea • Pyrexia • CPK elevation, muscle weakness, and rhabdomyolysis

Key to Abbreviations: BID = twice daily, CPK = creatine phosphokinase, HSR = hypersensitivity reaction, RAL = raltegravir, UGT = uridine diphosphate gluconyltransferase

Appendix B, Table 5. Characteristics of Fusion Inhibitor (Last updated January 29, 2008; last reviewed March 27, 2012)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendation	Serum/ Half-life	Elimination	Storage	Adverse Events (Also see Table 13)
Enfuvirtide (T20)/ Fuzeon	• Injectable—supplied as lyophilized powder • Each vial contains 108 mg of T20; reconstitute with 1.1mL of sterile water for injection for delivery of approximately 90 mg/1 mL.	90 mg (1mL) subcutaneously BID	3.8 hrs	Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool	Store at room temperature (up to 25ºC or 77ºF). Reconstituted solution should be refrigerated at 2ºC–8ºC (36ºF–46Fº) and used within 24 hours.	• Local injection site reactions (pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) in almost 100% of patients • Increased incidence of bacterial pneumonia • HSR (<1% of patients): Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. Rechallenge is not recommended.

Key to Abbreviations: BID = twice daily, HSR = hypersensitivity reaction, T20 = enfuvirtide

Appendix B, Table 6. Characteristics of CCR5 Antagonist (Last updated March 27, 2012; last reviewed March 27, 2012)

Generic Name (abbreviation)/ Trade Name	Formulation	Dosing Recommendations (For dosage adjustment in hepatic insufficiency, see Appendix B, Table 7.)	Serum/ Half-life	Elimination	Adverse Events (Also see Table 13)
Maraviroc (MVC)/ Selzentry	150-, 300-mg tablets	• **150 mg BID** when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers) including PIs (except TPV/r) • **300 mg BID** when given with NRTIs, T20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • **600 mg BID** when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take without regard to meals	14–18 hrs	CYP3A4 substrate	• Abdominal pain • Cough • Dizziness • Musculoskeletal symptoms • Pyrexia • Rash • Upper respiratory tract infections • Hepatotoxicity which may be preceded by severe rash or other signs of systemic allergic reactions • Orthostatic hypotension especially in patients with severe renal insufficiency

Key to Abbreviations: BID = twice daily; CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; T20 = enfuvirtide; TPV/r = tipranavir + ritonavir

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated March 27, 2012; last reviewed March 27, 2012) (page 1 of 4)

See reference section following tables for creatinine clearance (CrCl) calculation formulas and criteria for Child-Pugh classification.

Antiretrovirals Generic Name (abbreviation)/ Trade Name	Usual Daily Dose (Refer to Appendix B, Tables 1–6 for additional dosing information.)	Dosing in Renal Insufficiency (Including with chronic ambulatory peritoneal dialysis and hemodialysis)	Dosing in Hepatic Impairment
Nucleoside Reverse Transcriptase Inhibitors **Use of fixed-dose combination NRTI (+/- NNRTI) of Atripla, Combivir, Complera, Trizivir, or Epzicom is not recommended in patients with CrCl <50 mL/min. Use of Truvada is not recommended in patients with CrCl <30 mL/min.**			
Abacavir (ABC)/ Ziagen	300 mg PO BID	No dosage adjustment necessary	**Child-Pugh Score** — **Dose** 5–6 — 200 mg BID (use oral solution) >6 — Contraindicated
Didanosine EC (ddI)/ Videx EC	**Body weight ≥60 kg:** 400 mg PO once daily **Body weight <60 kg**: 250 mg PO once daily	**CrCl (mL/min)** — **Dose (once daily) ≥60 kg** — **<60 kg** 30–59 — 200 mg — 125 mg 10–29 — 125 mg — 125 mg <10, HD, CAPD — 125 mg — use oral solution	No dosage adjustment necessary
Didanosine oral solution (ddI)/ Videx	**Body weight ≥60 kg:** 200 mg PO BID or 400 mg PO once daily **Body weight <60 kg:** 250 mg PO once daily or 125 mg PO BID	**CrCl (mL/min)** — **Dose (once daily) ≥60 kg** — **<60 kg** 30–59 — 200 mg — 150 mg 10–29 — 150 mg — 100 mg <10, HD, CAPD — 100 mg — 75 mg	No dosage adjustment necessary
Emtricitabine (FTC)/ Emtriva	200-mg oral capsule once daily; or 240-mg (24-mL) oral solution once daily	**Dose** **CrCl (mL/min)** — **Capsule** — **Solution** 30–49 — 200 mg q48h — 120 mg q24h 15–29 — 200 mg q72h — 80 mg q24h <15 or HD — 200 mg q96h — 60 mg q24h On dialysis days, take dose after HD session.	No dosage recommendation
Lamivudine (3TC)/ Epivir	300 mg PO once daily; or 150 mg PO BID	**CrCl (mL/min)** — **Dose** 30–49 — 150 mg q24h 15–29 — 1 x 150 mg, then 100 mg q24h 5–14 — 1 x 150 mg, then 50 mg q24h <5 or HD — 1 x 50 mg, then 25 mg q24h On dialysis days, take dose after HD session.	No dosage adjustment necessary

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated March 27, 2012; last reviewed March 27, 2012) (page 2 of 4)

Antiretrovirals Generic Name (abbreviation)/ Trade Name	Usual Daily Dose (Refer to Appendix B, Tables 1–6 for additional dosing information.)	Dosing in Renal Insufficiency (Including with chronic ambulatory peritoneal dialysis and hemodialysis)	Dosing in Hepatic Impairment
Stavudine (d4T)/ Zerit	**Body weight ≥60 kg:** 40 mg PO BID **Body weight <60 kg:** 30 mg PO BID	**Dose** **CrCl (mL/min)** / **≥60 kg** / **<60 kg** 26–50 / 20 mg q12h / 15 mg q12h 10–25 or HD / 20 mg q24h / 15 mg q24h On dialysis days, take dose after HD session.	No dosage recommendation
Tenofovir (TDF)/ Viread	300 mg PO once daily	**CrCl (mL/min)** / **Dose** 30–49 / 300 mg q48h 10–29 / 300 mg twice weekly (every 72–96 hr) <10 not on HD / no recommendation HD / 300 mg q7d On dialysis days, take dose after HD session.	No dosage adjustment necessary
Emtricitabine (FTC) + **Tenofovir** (TDF)/ Truvada	1 tablet PO once daily	**CrCl (mL/min)** / **Dose** 30–49 / 1 tablet q48h <30 or HD / not recommended	No dosage recommendation
Zidovudine (AZT, ZDV)/ Retrovir	300 mg PO BID	**CrCl (mL/min)** / **Dose** <15 or HD / 100 mg TID or 300 mg once daily On dialysis days, take dose after HD session.	No dosage recommendation
Non-Nucleoside Reverse Transcriptase Inhibitors			
Delavirdine (DLV)/ Rescriptor	400 mg PO TID	No dosage adjustment necessary	No dosage recommendation; use with caution in patients with hepatic impairment.
Efavirenz (EFV)/ Sustiva	600 mg PO once daily at or before bedtime	No dosage adjustment necessary	No dosage recommendation; use with caution in patients with hepatic impairment.
Efavirenz (EFV) + **Tenofovir** (TDF) + **Emtricitabine** (FTC) Atripla	1 tablet PO once daily	Not recommended for use in patients with CrCl <50 mL/min. Instead use individual drug components of the fixed-dose combination and adjust TDF and FTC doses according to CrCl level.	
Etravirine (ETR)/ Intelence	200 mg PO BID	No dosage adjustment necessary	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no dosage recommendation
Nevirapine (NVP)/ Viramune or Viramune XR	200 mg PO BID or 400 mg PO once daily (using Viramune XR formulation)	Patients on HD: limited data; no dosage recommendation	Child-Pugh Class A: no dosage adjustment Child-Pugh Class B or C: contraindicated

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated March 27, 2012; last reviewed March 27, 2012) (page 3 of 4)

Antiretrovirals Generic Name (abbreviation)/ Trade Name	Usual Daily Dose (Refer to Appendix B, Tables 1–6 for additional dosing information.)	Dosing in Renal Insufficiency (Including with chronic ambulatory peritoneal dialysis and hemodialysis)	Dosing in Hepatic Impairment
Rilpivirine (RPV)/ Edurant	25 mg PO once daily	No dosage adjustment necessary	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no dosage recommendation
Rilpivirine (RPV) + **Tenofovir** (TDF) + **Emtricitabine** (FTC)/ Complera	1 tablet PO once daily	Not recommended for use in patients with CrCl <50 mL/min. Instead use individual drug components of the fixed-dose combination and adjust TDF and FTC doses levels according to CrCl level.	Child-Pugh Class A or B: no dosage adjustment Child-Pugh Class C: no dosage recommendation
Protease Inhibitors			
Atazanavir (ATV)/ Reyataz	400 mg PO once daily or (ATV 300 mg + RTV 100 mg) PO once daily	No dosage adjustment for patients with renal dysfunction not requiring HD ARV-naive patients on HD: (ATV 300 mg + RTV 100 mg) once daily ARV-experienced patients on HD: ATV or RTV-boosted ATV not recommended	**Child-Pugh Class** / **Dose** B: 300 mg once daily C: not recommended RTV boosting is **not** recommended in patients with hepatic impairment (Child-Pugh Class B or C).
Darunavir (DRV)/ Prezista	(DRV 800 mg + RTV 100 mg) PO once daily (ARV-naive patients only) or (DRV 600 mg + RTV 100 mg) PO BID	No dosage adjustment necessary	Mild-to-moderate hepatic impairment: no dosage adjustment Severe hepatic impairment: not recommended
Fosamprenavir (FPV)/ Lexiva	1400 mg PO BID or (FPV 1400 mg + RTV 100–200 mg) PO once daily or (FPV 700 mg + RTV 100 mg) PO BID	No dosage adjustment necessary	**Child-Pugh Score** / **Dose** PI-naive patients only: 5–9: 700 mg BID 10–15: 350 mg BID PI-naive or PI-experienced patients: 5–6: 700 mg BID + RTV 100 mg once daily 7–9: 450 mg BID + RTV 100 mg once daily 10–15: 300 mg BID + RTV 100 mg once daily
Indinavir (IDV)/ Crixivan	800 mg PO q8h	No dosage adjustment necessary	Mild-to-moderate hepatic insufficiency because of cirrhosis: 600 mg q8h

Appendix B, Table 7. Antiretroviral Dosing Recommendations in Patients with Renal or Hepatic Insufficiency (Last updated March 27, 2012; last reviewed March 27, 2012) (page 4 of 4)

Antiretrovirals Generic Name (abbreviation)/ Trade Name	Usual Daily Dose (Refer to Appendix B, Tables 1–6 for additional dosing information.)	Dosing in Renal Insufficiency (Including with chronic ambulatory peritoneal dialysis and hemodialysis)	Dosing in Hepatic Impairment
Lopinavir/ ritonavir (LPV/r) Kaletra	400/100 mg PO BID or 800/200 mg PO once daily	Avoid once-daily dosing in patients on HD	No dosage recommendation; use with caution in patients with hepatic impairment.
Nelfinavir (NFV)/ Viracept	1250 mg PO BID	No dosage adjustment necessary	Mild hepatic impairment: no dosage adjustment Moderate-to-severe hepatic impairment: do not use
Ritonavir (RTV)/ Norvir	As a PI-boosting agent: 100–400 mg per day	No dosage adjustment necessary	Refer to recommendations for the primary PI.
Saquinavir (SQV)/ Invirase	(SQV 1000 mg + RTV 100 mg) PO BID	No dosage adjustment necessary	Mild-to-moderate hepatic impairment: use with caution Severe hepatic impairment: contraindicated
Tipranavir (TPV)/ Aptivus	(TPV 500 mg + RTV 200 mg) PO BID	No dosage adjustment necessary	Child-Pugh Class A: use with caution Child-Pugh Class B or C: contraindicated
Fusion Inhibitor			
Enfuvirtide (T20)/ Fuzeon	90 mg subcutaneous BID	No dosage adjustment necessary	No dosage adjustment necessary
CCR5 Antagonist			
Maraviroc (MVC)/ Selzentry	The recommended dose differs based on concomitant medications and potential for drug-drug interactions. See Appendix B, Table 6 for detailed dosing information.	**CrCl <30 mL/min or HD** Without potent CYP3A inhibitors or inducers: 300 mg BID; reduce to 150 mg BID if postural hypotension occurs With potent CYP3A inducers or inhibitors: not recommended	No dosage recommendations. Concentrations will likely be increased in patients with hepatic impairment.
Integrase Inhibitor			
Raltegravir (RAL)/ Isentress	400 mg BID	No dosage adjustment necessary	Mild-to-moderate hepatic insufficiency: no dosage adjustment necessary Severe hepatic insufficiency: no recommendation

Key to Abbreviations: 3TC = lamivudine, ABC = abacavir, ARV = antiretroviral, ATV = atazanavir, AZT = zidovudine, BID = twice daily, CAPD = chronic ambulatory peritoneal dialysis, CrCl = creatinine clearance, CYP = cytochrome P, d4T = stavudine, ddI = didanosine, DLV = delavirdine, DRV = darunavir, EC = enteric coated, EFV = efavirenz, ETR = etravirine, FPV = fosamprenavir, FTC = emtricitabine, hr = hour, HD = hemodialysis, IDV = indinavir, LPV/r = lopinavir/ritonavir, MVC = maraviroc, NFV = nelfinavir, NNRTI = non-nucleoside reverse transcriptase inhibitor, NRTI = nucleoside reverse transcriptase inhibitor, NVP = nevirapine, PI = protease inhibitor, PO = orally, RAL = raltegravir, RPV = rilpivirine, RTV = ritonavir, SQV = saquinavir, T20 = enfuvirtide, TDF = tenofovir, TID = three times daily, TPV = tipranavir, XR = extended release, ZVD = zidovudine

Creatinine Clearance Calculation			
Male:	$\frac{(140 - \text{age in years}) \times \text{weight (kg)}}{72 \times \text{Serum Creatinine}}$	Female:	$\frac{(140 - \text{age in years}) \times \text{weight (kg)} \times 0.85}{72 \times \text{Serum Creatinine}}$

Child-Pugh Score			
Component	**Points Scored**		
	1	2	3
Encephalopathy[a]	None	Grade 1–2	Grade 3–4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory despite diuretics
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
Total bilirubin or	<2 mg/dL (<34 µmol/L)	2–3 mg/dL (34 µmol/L to 50 µmol/L)	>3 mg/dL (>50 µmol/L)
Modified total bilirubin[b]	<4 mg/dL	4–7 mg/dL	>7 mg/dL
Prothrombin time (seconds prolonged) or	<4	4–6	>6
International normalized ratio (INR)	<1.7	1.7–2.3	>2.3

[a] Encephalopathy Grades

Grade 1: Mild confusion, anxiety, restlessness, fine tremor, slowed coordination
Grade 2: Drowsiness, disorientation, asterixis
Grade 3: Somnolent but rousable, marked confusion, incomprehensible speech, incontinence, hyperventilation
Grade 4: Coma, decerebrate posturing, flaccidity

[b] Modified total bilirubin used for patients who have Gilbert's syndrome or who are taking indinavir or atazanavir

Child-Pugh Classification	Total Child-Pugh Score[c]
Class A	5–6 points
Class B	7–9 points
Class C	>9 points

[c] Sum of points for each component

Appendix C, Table 1. Monthly Average Wholesale Price[a] of Antiretroviral Drugs (Last updated March 27, 2012; last reviewed March 27, 2012) (page 1 of 2)

Antiretroviral Drug Generic (Brand) Name	Strength	Dosing	Tabs/Capsules/ mLs per Month	AWP[a] (Monthly)
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
abacavir (Ziagen)	300-mg tab 20-mg/mL soln	2 tabs daily 30 mLs daily	60 tabs 900 mL	$641.50 $674.60
didanosine DR (generic product) (Videx EC)	400-mg cap 400-mg cap	1 cap daily 1 cap daily	30 caps (≥ 60 kg) 30 caps (≥ 60 kg)	$368.72 $460.14
emtricitabine (Emtriva)	200-mg cap	1 cap daily	30 tabs	$504.37
lamivudine (generic) (Epivir) (Epivir)	300-mg tab 300-mg tab 10-mg/mL soln	1 tab daily 1 tab daily 30 mL daily	30 tabs 30 tabs 900 mL	$429.66 $477.41 $509.28
stavudine (generic) (Zerit)	40-mg cap 40-mg cap	1 cap twice daily 1 cap twice daily	60 caps 60 caps	$411.16 $493.38
tenofovir (Viread)	300-mg tab	1 tab daily	30 tabs	$873.28
zidovudine (generic) (Retrovir)	300-mg tab 300-mg tab	1 tab twice daily 1 tab twice daily	60 tabs 60 tabs	$360.97 $557.83
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
delavirdine (Rescriptor)	200-mg tab	2 tabs three times daily	180 tabs	$365.45
efavirenz (Sustiva)	200-mg cap 600-mg tab	3 caps daily 1 tab daily	90 caps 30 tabs	$689.52 $689.52
etravirine (Intelence)	100-mg tab 200-mg tab	2 tabs twice daily 1 tab twice daily	120 tabs 60 tabs	$978.64 $978.64
nevirapine (Viramune) nevirapine XR (Viramune XR)	200-mg tab 400-mg tab	1 tab twice daily 1 tab daily	60 tabs 30 tabs	$723.08 $632.68
rilpivirine (Edurant)	25-mg tab	1 tab daily	30 tabs	$804.38
Protease Inhibitors (PIs)				
atazanavir (Reyataz)	150-mg cap[b] 200-mg cap 300-mg cap[b]	2 caps daily 2 caps daily 1 cap daily	60 caps 60 caps 30 caps	$1,176.23 $1,176.23 $1,165.12
darunavir (Prezista)	400-mg tab[b] 600-mg tab[b]	2 tabs daily 1 tab twice daily	60 tabs 60 tabs	$1,230.20 $1,230.20
fosamprenavir (Lexiva)	700-mg tab	2 tabs twice daily 1 tab twice daily[b] 2 tabs once daily[b]	120 tabs 60 tabs 60 tabs	$1,812.68 $906.34 $906.34
indinavir (Crixivan)	400-mg cap	2 caps three times daily 2 caps twice daily[b]	180 caps 120 caps	$548.12 $365.41
nelfinavir (Viracept)	625-mg tab	2 tabs twice daily	120 tabs	$879.84
ritonavir (Norvir)	100-mg tab	1 tab once daily 1 tab twice daily 2 tabs twice daily	30 tabs 60 tabs 120 tabs	$308.60 $617.20 $1,234.40

Appendix C, Table 1. Monthly Average Wholesale Price[a] of Antiretroviral Drugs (Last updated March 27, 2012; last reviewed March 27, 2012) (page 2 of 2)

Antiretroviral Drug Generic (Brand) Name	Strength	Dosing	Tabs/Capsules/ mLs per Month	AWP[a] (Monthly)
saquinavir (Invirase)	500-mg tab[b]	2 tabs twice daily	120 tabs	$1,088.84
tipranavir (Aptivus)	250-mg cap[b]	2 caps twice daily	120 caps	$1,335.14
Integrase Strand Transfer Inhibitor (INSTI)				
raltegravir (Isentress)	400-mg tab	1 tab twice daily	60 tabs	$1,171.30
Fusion Inhibitor				
enfuviritide (Fuzeon)	90-mg inj kit	1 inj twice daily	60 doses (1 kit)	$3,248.72
CCR5 Antagonist				
maraviroc (Selzentry)	150-mg tab 300-mg tab	1 tab twice daily 1 tab twice daily	60 tabs 60 tabs	$1,148.16 $1,148.16
Coformulated Combination Antiretroviral Drugs				
abacavir/lamivudine (Epzicom)	600/300-mg tab	1 tab daily	30 tabs	$1,118.90
tenofovir/emtricitabine (Truvada)	300/150-mg tab	1 tab daily	30 tabs	$1,391.45
zidovudine/lamivudine (generic) (Combivir)	300/150-mg tab 300/150-mg tab	1 tab twice daily 1 tab twice daily	60 tabs 60 tabs	$931.61 $1,035.12
abacavir/lamivudine/zidovudine (Trizivir)	600/150/300-mg tab	1 tab twice daily	60 tabs	$1,676.62
lopinavir/ritonavir (Kaletra)	200 mg/50-mg tab 400 mg/100 mg per 5-mL soln	2 tabs twice daily or 4 tabs once daily 5 mL twice daily	120 tabs 300 mL	$871.36 $871.34
rilpivirine/tenofovir/emtricitabine (Complera)	200/25/300 mg	1 tab daily	30 tabs	$2,195.83
efavirenz/tenofovir/emtricitabine (Atripla)	300/200/600 mg	1 tab daily	30 tabs	$2,080.97

[a] AWP = Average Wholesale Price in 2012 (source: First DataBank Blue Book AWP, accessed January 2012) Note that this price may not represent the pharmacy acquisition price or the price paid by consumers.

[b] Should be used in combination with ritonavir. Please refer to Appendix B, Table 3 for ritonavir doses.

Key to Abbreviations: AWP = average wholesale price; cap = capsule, DR = delayed release, EC = enteric coated, inj = injection, soln = solution, tab = tablet, XR = extended release